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THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE HISTORY OF THE FERTILIZATION PROBLEM[1]

WE come together at this season of the year to discuss the latest advances in our science and to listen to the announcement of new discoveries. This implies a philosophy of life, an optimistic philosophy; we would not work as individuals nor assemble as societies if we did not believe that science is worth while, and that human progress is both possible, and, for some inscrutable reason, worth working for. This was the philosophy of science in the time of the Greeks, and it is the philosophy of our science of scarce four hundred years' growth. Modern science, I need hardly say, was entirely European in its origin, as is our American scientific population; and all science is ours to promote and advance by right of inheritance no less than of intellectual sympathy. Now that the great war is so largely arresting the progress of science in Europe it is our bounden duty to see that there is no halting in America; we should hold fast to our faith and strengthen our efforts for the advancement of science.

As we all labor for progress in science, I thought it would not be entirely out of place if, instead of dealing with some new subject, I attempted to lay before you a picture of the total progress in some central problem of biology; it can be nothing more than a sketch, but it may perhaps

[1] Address delivered before the American Society of Naturalists, and the Zoological Section of the American Association for the Advancement of Science, December 30, 1915.

help to justify our faith, and also to temper our conceit, if we have any. Fertilization is such a central problem which has interested mankind from the dawn of reasoning on account of its fundamental character, and is more or less interwoven with the thought of all ages.

Aristotle and Harvey.—It must be remembered in beginning our topic that the problem of fertilization was not clearly separated from the general problem of reproduction until well into the nineteenth century. In early human culture reproduction received its only interpretation at the hands of priests and mystery men; its first philosophical and scientific treatment was one of the great distinctions of the Greeks, especially of that great philosopher and father of science, Aristotle, who combined observation and reflection in the interpretation of nature. Aristotle devoted a separate treatise, which has come down to us, to animal reproduction. Among other things he studied the development of the chick day by day with so much detail that Harvey felt impelled to say, 1,900 years later:

> Aristotle among the ancients, and Hieronymus Fabricius of Aquapendente, among the moderns, have written with so much accuracy on the generation and formation of the chick from the egg that little seems left for us to do.

From the time of the Greeks to that of Harvey (1651) there was but little progress in the knowledge of reproduction, and none in the theory, as will appear from the views of Aristotle, the current views of medical men of Harvey's time, and of Harvey himself. Aristotle says:[2]

> The male is the efficient agent, and by the motion of his generative virtue (genitura), creates what is intended from the matter contained in the female; for the female always supplies the matter, the male the power of creation, and this it is which constitutes one male, another female. The body and the bulk, therefore, are necessarily supplied by the female; nothing of the kind is required from the male; for it is not even requisite that the instrument, nor the efficient agent itself, be present in the thing that is produced. The body then proceeds from the female, the vital principle (anima) from the male; for the essence of every body is its vital principle (anima).

With more common sense, if with less metaphysical subtlety, the physicians of the Middle Ages held, according to Harvey, that conception is due to a mingling of male and female seminal fluids,

> the mixture having from both equally the faculty of action and the force of matter; and according to the predominance of this or that geniture does the progeny turn out male or female (quoted from Harvey, Ex. 32).

Harvey's observations contained much that was new and significant, but the facts that he knew were inconsistent both with Aristotle's ideas and those of the physicians. They were, however, inadequate for sound generalization.

> Wandering between two worlds, one dead
> The other powerless to be born,

he descended deeper into the slough of metaphysics than Aristotle, and committed himself to the fantastic idea that conception in the uterus is identical with, or at least analogous to, conception in the brain; and that the ovum is the product of such unconscious uterine desire or conception, and receives no material substratum from the male![3] The theory of reproduction

[2] "De Gen. Anim.," lib. II., cap. 4, quoted from Harvey "On the Generation of Animals," Ex. 29.

[3] "Since there are no manifest signs of conception before the uterus begins to relax, and the white fluid or slender threads (like the spider's web) constituting the 'primordium' of the future 'conception' or ovum, shows itself; and since the substance of the uterus, when ready to conceive, is very like the structure of the brain, why should we not suppose that the function of both is similar, and that there is excited by coitus within the uterus a something identical with, or at least analogous to, an 'imagination' (phantasma) or a 'desire' (appetitus) in the brain, whence comes

was no whit more advanced in the middle of the seventeenth century than in the time of Aristotle.

The Period of Leeuwenhoek.—The use of the microscope in biological research began in the seventeenth century; it was the improvement of this new instrument of investigation and its application to the study of the reproductive substances that furnished the first fundamental advance in the theory of reproduction at the hands of Leeuwenhoek, viz., the discovery of the spermatozoa[4] in 1677.

This discovery aroused the greatest interest in scientific circles; a number of investigators repeated the observations and a spirit of speculation which led to wild flights of the imagination was aroused. Leeuwenhoek had soon to defend his priority in the matter and to protest against certain very imaginative views. Thus in a letter dated June 9, 1699,[5] he defends his priority and combats the notion that the human form can be observed in the spermatozoa. He inveighs especially against a certain Dr. Dalen Patius, who claimed to have seen the human form,

> the two naked thighs, the legs, the breast, both arms, etc., the skin being pulled up somewhat higher did cover the head like a cap.

Leeuwenhoek states that he can find nothing of the sort, but he adds:

> I put this down as a certain truth, that the shape of the human body is included in an animal of the masculine seed; but that a man's reason shall dive or penetrate into this mystery so far, that in anatomizing one of these animals of the masculine seed we should be able to discover the entire shape of the human body, I can not comprehend.

In a letter dated two weeks later he distinguishes two sorts of these animalcules, and concludes that the one sort is male and the other female.

this observation and repeated it many times. In this letter he gives a fair description of the spermatozoa, their form, size and movements and stated that he had observed them three or four years previously and mistaken them for globules. He did not at this time speculate as to the meaning of the spermatozoa, but in true scientific spirit began to make comparative observations, and in 1678 he described and figured spermatozoa of the rabbit and frog among others.

The credit of this discovery seems to me to belong rightly to the investigator whose wide experience in the field of microscopical anatomy and whose scientific acumen enabled him to grasp the possible significance of the discovery; not to the chance observer who called Leeuwenhoek's attention anew to the subject.

> the generation or procreation of the ovum. For the functions of both are termed 'conceptions,' and both, although the primary sources of every action throughout the body, are immaterial, the one of natural or organic, the other of animal actions; the one (viz., the uterus) the first cause and beginning of every action which conduces to the generation of the animal, the other (viz., the brain) of every action done for its preservation. And just as a 'desire' arises from a conception of the brain, and this conception springs from some external object of desire, so also from the male, as being the more perfect animal, and, as it were, the most natural object of desire, does the natural (organic) conception arise in the uterus, even as the animal conception does in the brain.
>
> "From this desire or conception, it results that the female produces an offspring like the father. For just as we, from the conception of the 'form' or 'idea' in the brain, fashion in our works a form resembling it, so, in like manner, the 'idea' or 'form' of the father existing in the uterus generates an offspring like himself with the aid of the formative faculty, impressing, however, on its work its own immaterial 'form'" (from William Harvey, "On Conception," 1651).

[4] This discovery is sometimes credited to Hamm, described as a student of Leeuwenhoek's. The latter himself describes the occurrence as follows (*Phil. Trans.*, 1678, containing a letter from L. dated November, 1677): A certain Professor Cranen, who had frequently visited Leeuwenhoek for microscopical demonstration, requested by letter that he should give Dominus Hamm, a relative of his, some demonstrations of his observations. On his second visit D. Hamm brought in a glass vial some seminal fluid and stated that he had observed living animals in it; Leeuwenhoek confirmed

[5] *Phil. Trans.*, Vol. 21.

In France in the year of 1694, Nicholas Hartsoeker claimed to have been the first to have discovered the spermatozoa more than twenty years previously, although he did not publish until 1678, a year later than Leeuwenhoek's publication. Hartsoeker's ideas are characterized by a high degree of precision. He believes that each spermatozoon conceals beneath its "tender and delicate skin" a complete male or female animal, "which would perhaps appear if it could be seen like the following figure."[6] The egg is merely a source of nourishment for the real germ contained in the spermatozoon. In birds the spermatozoon enters an egg to be nourished; there is but a single opening in the egg, situated over the so-called germ, and this opening closes after a single spermatozoon is admitted; but if two spermatozoa enter they unite and form a double monster. In mammals the tail of the spermatozoon is the umbilical cord; this unites with the ovum, *i. e.*, the placenta, and the latter with the uterus. Each one of male animals (spermatozoa) encloses an infinity of other animals both male and female, which are correspondingly small, and those male animals enclose yet other males and females of the same species, and so forth in a series which includes all the members of the species which are to be produced up to the end of time. No difficulty was found in this conception, for the atomic theory of matter was not yet placed on a scientific basis.

Thus was founded and flourished for its brief day the school of the spermatists. Unhampered by any scientific conception of matter, living or non-living, there was no obstacle to the eye of faith and no impediment to the age-old longing to make an intelligible universe out of the scraps of experience.

[6] The figure in question is reproduced in Kellicott's General Embryology, p. 22.

The Period of Spallanzani.—In the entire eighteenth century, although speculation continued rife, there was only one notable contribution to our subject. This was the work of the Abbé Spallanzani, "Expériences pour servir à l'histoire de la génération des Animaux et des Plantes," published in Geneva in 1785. His working hypotheses were naturally in the spirit of the times. Theories of reproduction, he says, may be reduced to two.

> The one explains the development of organisms mechanically, the other supposes them to preexist, and waiting only for fertilization to develop them. The second system has given birth to two different parties, one believing that the organism is preformed in the ovum, the other that it is preformed in the spermatozoon.

Spallanzani believed that his observations destroyed the epigenetic theory as propounded by Buffon and others, because they demonstrated the existence of the fetuses (ova) in the females of toads, frogs and salamanders, prior to the act of fertilization, which according to the epigenesists animates or creates the germ. For the same reason the spermatists must also be wrong. Spallanzani thus combated epigenesis as understood in the eighteenth century, and also the ideas of the spermatists, and he was led to deny that spermatozoa are necessary for fertilization, and to hold that the fertilizing power of the seminal fluid resides not in the spermatozoa, but in the fluid medium that accompanies them; and this in spite of the fact that his final experiments really proved the reverse.

His work contains a great wealth of observation and experiment, so that it will be possible merely to indicate some of his chief results. In the first place he demonstrated that in frogs and toads fertilization takes place outside of the body, and for the first time he successfully carried out artificial insemination, thus laying the foundation for the artificial propagation of many ani-

mals. In making these experiments he thought he found cases in which seminal fluid devoid of spermatozoa would fertilize and thus fell into the error, which he was so ready to accept from his opposition to the spermatists, that the fluid medium of the seminal fluid was the fertilizing substance. He also investigated the conditions of successful insemination, with reference to the duration of fertilizing power, exposure to various chemicals, to heat, etc. The amount of dilution of which the seminal fluid was capable was also carefully investigated. By experiment he excluded the idea that fertilization might be an effect of an emanation, or vapor arising from the sperm.

He concluded that the seminal fluid acted by accelerating the vital processes; it enters the body through pores, and stimulates the action of the heart. This idea offered no difficulty to one who believed that the organism was preformed in the ovum, and it was supported by the observation that the beating of the heart was the first observable movement of the embryo. Bonnet suggested to him the problem, if the spermatic fluid might stimulate the heart of the embryo in the process of fertilization, why might not other fluids produce the same effect? He was thus led to attempt the first experiments on artificial parthenogenesis; he tried to start the development of eggs by electricity, by the action of extracts of all the various organs, by vinegar, dilute alcohol, lemon juice, and other substances, all without effect.

It is interesting to see how his experiments led to hypotheses and these, even though wrong, to further experiments, some of which, like his experiments on artificial parthenogenesis, were not taken up again in a fruitful way for over a century.

His final experiments are those so often quoted as furnishing the proof that fertilizing power resides in the spermatozoon. He showed that, if diluted sperm be filtered through a sufficient number of layers of filter paper, the filtrate has no fertilizing power, whereas the residue washed off the filter paper will fertilize. But he did not himself draw the correct conclusion; he says the experiment proves "that filtration removes from spermatized water its fertilizing power, inasmuch as the seminal fluid which was contained in it remains on the filter papers, from which one can extract it by pressing them." It is perfectly clear that Spallanzani himself never held that the spermatozoa themselves were the fertilizing agents, but, on the contrary, he contests this idea strongly as leading to spermatist delusions.

1800–1870.—After Spallanzani there was no real advance in the theory of fertilization until the publication of Prevost et Dumas' "New Theory of Reproduction" in 1824. They observed that young animals incapable of breeding, old animals beyond the breeding stage, the infertile mule, and birds outside of the breeding season possess no spermatozoa, and they conclude that these facts "sufficiently prove the importance of the animalcules, and show that there exists an intimate relationship between their presence in the reproductive organs and the fertilizing power of the animal." In a long series of experiments they investigated the conditions of fertilization in frogs: all conditions that destroy the animalcules destroy also the fertilizing power of sperm suspensions; the filtrate of a sperm suspension devoid of spermatozoa will not fertilize; the redissolved residue of a suspension evaporated to dryness will not fertilize, etc.; the number of eggs fertilized is always less than the number of animalcules employed. So that they came to the conclusion that "the prolific principle resides in the spermatic animalcules."

In their subsequent publications they concluded that it is

> infinitely probable that the number of animalcules employed in fertilization corresponds to that of the embryos developed . . . so that the action of these animalcules which we regard as the male reproductive elements is individual, not collective.

They concluded that a spermatozoon penetrates each egg and becomes "the rudiment of the nervous system, and that the membrane (germ disc of the egg) in which it is implanted, furnishes, by the diverse modifications which it undergoes, all the other organs of the embryo."

These studies gave a new impetus to the study of fertilization; some were convinced that Prevost et Dumas were essentially correct, while others still adhered to the idea that the fluid part of the seminal fluid was the fertilizing medium. Thus the celebrated embryologist Bischoff in 1842 does not hesitate to declare outright for the latter view "that only the dissolved part of the semen penetrates into the egg and thus completes fertilization." He considered that

> Valentin's hypothesis united all the facts; the seminal fluid is so unstable chemically as to break down as soon as the particles come to rest; it is similar to the blood in this respect, but it is not in regular circulation and the function of maintaining its chemical composition is relegated to the movements of the spermatozoa.

However, Bischoff subsequently became convinced that the spermatozoa were themselves the essential agents, though he still refused to believe in the penetration of the egg. Kölliker had put forward a contact theory of fertilization, which Bischoff regarded merely as a statement of facts requiring further development. He therefore adopted the idea of catalyzers, at that time a new idea in chemistry, and held that the spermatozoon was essentially a catalytic agent, *i. e.*, as he defined it, "a form of matter characterized by definite transformation and internal movement" which it transmits by contact to the egg, which is in a condition of maximum tension or inclination to assume the same form of transformation and movement. Fertilization is thus not a process of union and fusion as in ordinary chemical combination, but a catalytic process, as defined above.

This point of view deserves to be emphasized as one of the first attempts at a physico-chemical explanation of fertilization.

For some time naturalists were divided between the two points of view, viz., that of Prevost et Dumas, that the sperm penetrated into the egg, and that of Kölliker and Bischoff that it acted by contact. Lallemand (1841) well expresses the view of those who believed in the union of the ovum and spermatozoon:

> Each of the sexes furnishes material already organized and living. . . . A fluid obviously can not transmit form and life which it does not possess. . . . Fertilization is the union of two living parts which mutually complete each other and develop in common. . . . When one embraces in a single point of view the reproduction of all living beings, one arrives at the following more general formula: Reproduction is the separation of a living part which may either develop separately or acquire from another living part the supplementary elements necessary for the ulterior development of a being similar to the type. . . . The preservation of the type is due to the extension of the same act which has produced the development of each individual being.

This is the most complete statement of the principle of genetic continuity that I have found in the literature of this period.

These observations and conclusions were found on the eve and early morrow of the greatest biological generalization, the cell-theory. Though Schwann interpreted the ovum as a cell (1838), this view did not at once become dominant, and was generally accepted only after over twenty years of discussion. The view that spermatozoa were parasitic organisms was more or less

current until Kölliker in 1841 showed by their development that they were modified cells. Nevertheless, there was, strictly speaking, no immediate application of these results to the problems of fertilization.

The half century from 1824 to 1874 yielded relatively little advance in fertilization theory; the opinion that the spermatozoon actually penetrated into the ovum gradually gained ground largely from the very logic of the situation, but partly from various observations. Bischoff's contact theory, which was the only alternative, was criticized because if the sperm does not penetrate, but remains outside of the membrane, there is absence of that direct contact between sperm and egg substance postulated by the theory. Wagner's criticism was also very effective; a ferment does not determine the character of a reaction, but the spermatozoon does, for it transmits paternal characteristics. In the way of observations Barry in 1840, Newport,[7] 1854–1855, Meissner, 1855, and others maintained observations of penetration of the ovum by the spermatozoon; Keber (1854) laid especial emphasis on the micropyle as adapted for entrance of a spermatozoon. These observations were on the whole inconclusive, for actual penetration was not observed, but inferred from the presence of spermatozoa inside the egg membrane. Moreover, the spermatozoon could not be discovered within the egg.

The Modern Period.—The preceding period (1824–1874) was coincident, as we have seen, with the early history of the cell theory, but the demonstration of the unicellular character of the ovum and spermatozoon had little effect upon the problems of fertilization. The cell theory was still incomplete; the free formation of the nuclei was still held by competent naturalists, and nothing was known of the phenomena of karyokinesis. The cytological investigations of the next ten years (1874–1884) were destined to lay the foundations of the modern nuclear theory in its broad outlines. The fertilization studies of this period were mainly morphological, and while it is correct to say that they were largely dominated by the growing nuclear theory, it is also strictly true that they contributed in no small measure to its upbuilding. Though the penetration of the spermatozoon into the egg had long been suspected, it was first clearly demonstrated in this time; the origin of the egg nucleus by two successive divisions of the germinal vesicle was discovered; the origin of the sperm nucleus from the head of the spermatozoon, the sperm aster, the union of the egg nucleus and the sperm nucleus, the relation of these to the first cleavage spindle, the origin of the fertilization membrane, the ill effects of polyspermy and the theory of its prevention; and finally the doctrine of the equivalence of the egg and sperm nuclei, and the biparental character of the nuclei of sexually produced organisms, as first laid down by Van Beneden, were products of the period also. No period of cytological research seems to me of greater significance than this.

There was almost a complete cessation of investigation from 1855–1873, when the dawn of the modern period broke suddenly. In 1873 Bütschli observed in the egg of a nematode the approach and contact of the two structures, which we now know to be the germ-nuclei, immediately preceding the first cleavage of the ovum. But no interpretation was presented. In 1874 Auer-

[7] Newport's observations rose to a higher plane than those of the others, for he actually observed in the frog's egg (1) that the first plane of cleavage is in line with the point on the egg artificially impregnated, (2) that it marks the plane of symmetry of the embryo, (3) that the head of the young frog is turned towards the same point.

bach[8] described the appearance of two nuclei at opposite ends of the elongated egg of Rhabdites; these increase in size, migrate towards the center of the egg, meet, rotate through 90° and fuse together. A dicentric figure appears and cleavage follows. What is the origin of these two nuclei and the significance of their union? The fusion of two nuclei was at the time entirely without analogy. Auerbach states:

> It is natural to assume that, as for the reproduction of organisms the copulation of two individuals, or at least of two cells in some form or other is so frequently necessary, so here a similar condition is found for nuclear reproduction.

Auerbach supposes the two nuclei which appear at opposite ends of the elongated egg to have arisen freely; one of these comes from the end where the spermatozoa had penetrated, the other from the opposite end where the germinal vesicle had disappeared. The difference of the origin influences the quality of the nuclear materials arising *de novo;* fusion of the nuclei counteracts the differences thus arising; but all this would be undone if the division of the fusion nucleus followed along the plane of the union; hence the rotation through 90°.

In the next year Bütschli again observed fusion of nuclei in nematode eggs before the first cleavage. However, he did not accept Auerbach's interpretation, but he tended to regard it as a general law of nuclear formation, that first two or several small nuclei arise and subsequently fuse; this he finds to occur even in the blastomeres of the four- and eight-cell stages.

About the same time (1875) Van Beneden also observed similar phenomena in the rabbit's egg. He did not see spermatozoa enter the egg, but he found them with their heads closely applied to the surface in every unsegmented egg, and came to the conclusion that fertilization consisted essentially in fusion of the spermatic substance with the superficial layer of the vitellus. At a little later stage he found a small nucleus in the cortical layer of the egg; this he called the peripheral pronucleus; a central pronucleus appeared simultaneously. They grow, approach one another and meet in the center. Later there is only one nucleus, probably formed by the union of the two.

> As I have shown that the spermatozoa attach to the surface of the vitellus and mix with its superficial layer, it appears probable to me that the superficial pronucleus is formed, partially at least, at the expense of the spermatic substance. If, as I think, the central pronucleus is constituted of elements furnished by the egg, the first nucleus of the embryo would be the result of union of male and female elements. I put forth this latter idea simply as a hypothesis, an interpretation which may or may not be accepted.

The way was now clear for the definitive solution of the old riddle of the relation of the egg and spermatozoon, which was quickly furnished by O. Hertwig and Hermann Fol. The observations of these authors appear to have been made independently and nearly simultaneously. In 1875 Hertwig observed and described correctly the principal phenomena of fertilization in the sea-urchin egg. He did not actually see the penetration of the spermatozoon, but he observed the sperm nucleus and its aster so soon after that he had no doubt of the correct interpretation; he also observed the approach of the sperm-nucleus and the egg-nucleus to the center of the egg and their apparent fusion.

> Fertilization has been previously interpreted as a fusion of two cells, but we have now seen that the most important process involved is the fusion of the two nuclei. The union of the egg-nucleus with the sperm-nucleus is necessary to produce a nucleus endowed with living forces adequate effectively to stimulate the later developmental processes in the yolk, and to control them in many respects.

Fol's observations, made partly independently of Hertwig's and partly after the

[8] "Organologische Studien."

publication of Hertwig's first paper, supplemented Hertwig's in several important respects: (1) He observed the details of penetration of the spermatozoon with a clearness that has never been surpassed for these forms. (2) He gave the first correct account of the maturation divisions and origin of the egg-nucleus (Hertwig regarded the latter as being the persistent nucleus of the germinal vesicle). (3) He paid special attention to the origin of the fertilization membrane and founded the classic theory that it was an adaptation to prevent polyspermy. (4) He was the first one adequately to present the harmful effects of polyspermy.

The period initiated by these two men was characterized mainly by the repeated demonstration of penetration of the spermatozoon, the formation of a nucleus from the sperm head, and the fusion of this nucleus with the egg-nucleus. It was also gradually demonstrated that the egg-nucleus is genetically derived from the germinal vesicle by karyokinetic divisions. Thus the genetic continuity of the germ nuclei with nuclei of preceding cell generations was established. As yet the character of the fusion of egg and sperm nuclei had hardly been raised, for the chromosome problems and hypotheses were in a very nascent state. Flemming's discoveries concerning chromosomes and their reproduction in karyokinesis by splitting date only from 1876–1878.

All the problems of cell morphology were in a fine state of fermentation during this time, the really classic period of cell-morphology; the foundations of our present knowledge of cell-division were being laid; before the decade 1870–1880 it had been firmly established that cells arise only by division from preexisting cells; but two views of the origin of nuclei were still held, one that of free formation, according to which the nuclei of daughter cells had no genetic connection with the nucleus of the mother cell, and the other that nuclei arise by division from a preceding nucleus. Little by little as a result of numerous investigations by many investigators, both zoologists and botanists, the matter cleared up. In 1878 Flemming was able to outline the whole scheme of karyokinesis substantially as we now understand it.

The fundamental biological principle of genetic continuity was foreshadowed by the founders of the cell doctrine, and was more or less distinctly foreseen by some of their contemporaries, as in the case of Lallemand. It was yet more clearly expressed in Virchow's famous aphorism, *omnis cellula e cellula* (1856); but it could not become an established guiding principle in genetic research until the entire cell-cycle of the individual life history was worked out in broad outline, until the process of cell division was accurately ascertained and applied to the genealogy of the germ-cells, until the respective parts of ovum and spermatozoon in the origin of the new generation were understood, nor until the hoary doctrine of spontaneous generation was banished bodily from the field of biology. These were all accomplishments of that great decade in biological research, 1870–1880, for which the studies of the preceding thirty years had furnished ample preparation. The entire superstructure of modern genetic research rests upon the foundations then laid.

Professor Mark's paper on *Limax* (1881) is a point of departure between the fertilization studies of the seventies and those that were to follow. Professor Mark observed that the pronuclei come together, but do not fuse to form a first cleavage nucleus, as had been described for other animals.

The first cleavage nucleus does not have a morphological existence.

The pronuclei persist after the appearance of the cleavage centers, their membranes then gradually disappear.

In 1883 van Beneden published his now classic paper on *Ascaris*: The pronuclei do not unite, both are included in a single amphiaster; each produces two chromosomes; these divide and their halves form the daughter nuclei. In the nuclei of the first two cells there are thus equal numbers of male and female elements, and there are reasons to believe that even in these two nuclei they do not fuse; it is probable that they remain distinct in all derivative cells, including the immature eggs and spermatogonia. In the egg the chromatin is composed of two distinct parts, and

> it is legitimate to suppose that each is the equivalent of a male and a female chromosome, and that in the formation of the polar globules each throws out the male chromatin which it contains.

Van Beneden by a veritable stroke of genius thus anticipates the entire chromosome doctrine of the present time, even though certain aspects of his interpretation were not entirely fortunate: his conception of the diploid cells as hermaphrodite, for instance, and freeing of egg and sperm from the male or female elements in maturation.

With the establishment of the nuclear theory, destined soon to be elevated into the doctrine of chromosome individuality, a certain duality of cell-life was recognized in which nucleus and cytoplasm, however interdependent, were regarded as playing specific rôles. But there was no logical reason for stopping at duality, and the centrosome soon came to be recognized under van Beneden and Boveri's leadership as a third organ of cell-life reproducing itself by division. The development of this idea was due not only to studies of karyokinesis, but also to the series of fertilization studies which began with Boveri's classic papers on *Ascaris* (1887–1888). In these papers Boveri is convinced of the necessity of making "the sharpest distinction between fertilization and heredity, *i. e.*, between the question how egg and spermatozoon produce a cell capable of division, and the question how these cells come to be capable of reproducing the qualities of the parents in the offspring"; this distinction has since been generally recognized. Boveri's solution of the fertilization problem was in terms of the centrosome hypothesis: the egg is devoid of the organ of cell-division, the centrosome; capacity for division, hence the initiation of the developmental processes, is restored through the introduction of a centrosome into the egg by the spermatozoon.

This conception exerted a dominating influence on the series of fertilization studies which followed; the questions as to the origin of the sperm aster with its contained centrosome in the egg, and as to the genetic continuity of the sperm centrosome with the centrosomes of the cleavage amphiaster were energetically investigated by a series of students for the next fifteen years or more, and similar studies have continued with less energy down to the present time. Collectively these publications constitute a fairly exhaustive record of the morphology of the fertilization process in animals, a large part of which was furnished by American students.

The morphological analysis of fertilization seems now to be fairly complete; there may still be disturbances such as recent attempts to trace mitochondria back to the sperm, which seems destined to share the adverse fate of the similar attempt to trace the centrosomes to the sperm; but there is not likely to be any great modification of the existing data, which seem to me to demonstrate, effectively if not absolutely, that the sperm head contains all the substances necessary for fertilization. We have thus

attained a more or less definitive solution of the morphological relations of egg and spermatozoon in the fertilization process.

The cytologist working with chromosomes and the geneticist with Mendelian factors have traced maternal and paternal elements through the life history in a manner very satisfactory to certain classes of biologists, however repugnant to others, so that we are beginning to see how certain strands of the web of life cross the gap of successive generations. It remains for the biology of the future to elucidate the chemical foundations of chromosome behavior and to identify the Mendelian factors in these chemical foundations.

The problems of the immediate reaction of the reproductive elements and the physiology of fertilization are not touched by this morphological analysis, though they had been present in the minds of investigators from the beginning. The experimental investigation of these problems dates from Spallanzani, as we have seen, but they did not become dominant until the morphological problems of fertilization were in an advanced stage of solution. They constitute, however, the more immediate problems of fertilization, considered in a restricted sense.

We have had two lines of attack since the studies of O. and R. Hertwig published in 1887 really initiated the modern period in the physiology of fertilization. The one is a direct experimental analysis of the fertilization process itself; the other is the attempt to imitate the action of the spermatozoon by chemical and physical agencies, in short the studies on artificial parthenogenesis. I shall not attempt to deal with the latter, which constitute one of the most interesting and suggestive chapters in modern biology, beyond attempting to define their relation to the problems of fertilization proper.

It was soon found in the course of studies on artificial parthenogenesis that no single physical or chemical agency suffices to initiate development in all eggs, and that when the various agencies effective in all the successful experiments are assembled they constitute a fairly complete list of agencies to which protoplasm in general is irritable. The idea then arose that the common factor must be the effective one, but no common factor has been found, or can be found, in the agents themselves; the only common factors are in the reproductive cells. This leaves the method of parthenogenesis in the same position as the method of analysis, that is in the position of determining what are the changes in the egg itself that initiate development, and what is the nature of their dependency upon the external agent or spermatozoon? The answer to these questions can not proceed exclusively from parthenogenetic studies, though to the extent that the same questions are involved parthenogenesis and fertilization studies must furnish the same answer. But there are obviously fundamental problems of fertilization that can not be touched by methods of artificial parthenogenesis.

The conditions to be fulfilled in fertilization involve not only penetration of the spermatozoon, or some part of it, into the egg, but also reaction between the two, which is evidenced by the behavior of both partners; for it is possible for a spermatozoon to penetrate an egg and no reaction to be evidenced in the behavior of either the egg or sperm; as when immature eggs are penetrated by mature spermatozoa. We may therefore speak of a *fertilization reaction* when the behavior of both partners indicates that the process is proceeding normally. Fertilization has its quantitative aspect, and the reaction may be complete or exhibit varying degrees of incomplete-

ness. For a normal fertilization reaction certain internal conditions of the partners and certain external conditions of the medium must be realized. The study of the external conditions throws light upon the reaction, because the nature of the internal conditions may be inferred from the necessary, from the inhibiting, and from the favoring conditions of the medium.

External Factors.—The fertilization reaction like all biological reactions requires certain conditions of the environment, such as definite range of temperature and chemical composition of the medium. In the first place, if these are exceeded in either direction so far as to injure the cells the fertilization reaction either does not take place, or it is rendered abnormal. The cause of the failure, or the abnormality, in such cases lies in some change of the internal composition of one or the other of the germ-cells. The classic experiments of this kind are those of Oskar and Richard Hertwig published in 1887. These investigators studied the effects of high temperature, various injurious chemical reagents and of mechanical shock on the germ-cells separately before fertilization, and on the process of fertilization itself at various stages. Many exceedingly interesting observations were made, and problems were raised that were not then ripe for solution. Other experiments of a similar kind have since been made, but their consideration properly belongs to the problems of the internal factors, for the phenomena observed depend upon internal changes of the germ-cells.

In the second place there may be modifications of the medium which do not directly injure the germ-cells, but which inhibit or favor the fertilization reaction. Examples of inhibiting phenomena are found in Professor Loeb's studies of the relations of ions to the fertilization reaction, or my own on the inhibiting action of blood or tissue secretions of the same species on fertilization. The most striking example of conditions favoring fertilization is the action of alkalis in enabling interclass hybridization, discovered by Jacques Loeb. Such experiments furnish important data for the analysis of the reaction, but it is obvious that their interpretation must depend upon internal conditions of the fertilization reaction.

In the third place the membranes of the egg and of the spermatozoon must influence the occurrence, rate and extent of the fertilization reaction according to the degree of their permeability to the substances concerned; the egg-membrane is of course more especially concerned; its rôle in the occurrence of parthenogenesis has been studied especially by R. S. Lillie; and I have found in the case of the starfish egg that a resistant egg-membrane may entirely block the fertilization reaction, though the block may be removed by agents that render the membrane more permeable.

The internal conditions of the fertilization reaction may be grouped under two heads: (1) Maturity of the germ-cells; (2) specificity of the reaction.

1. *Maturity.*—Concerning conditions of maturity of the spermatozoon but little definite is known, except that it will not fertilize before its differentiation is complete. Whether the cause of this lies entirely in deficient motility, or partly also in incomplete chemical differentiation, we do not know; though there are some reasons for thinking that the latter factor may be involved. In the case of the ovum our knowledge is in a much more advanced stage. We know that the fertilizable condition, which represents the final maturity of the ovum, arises rather suddenly, usually lasts but a short time, and is lost as an immediate consequence of the fertilization reaction. (*a*)

That the fertilizable condition arises suddenly has been shown especially by the work of Délage on the starfish egg and of Wilson on the egg of *Cerebratulus*. Their experiments on merogony showed that parts of the full-grown ovum taken prior to the rupture of the germinal vesicle are incapable of fertilization; but, soon after the rupture of the germinal vesicle, parts, whether nucleated or not, readily fertilize. Hertwig's observations (1877) also showed a complete failure of the fertilization reaction in primary ovocytes of the sea-urchin before rupture of the germinal vesicle, even when spermatozoa penetrated. I have observed the same thing in *Chætopterus*.

(*b*) Eggs of *Platynereis* lose their capacity for fertilization almost immediately after coming into sea water, even though spermatozoa may penetrate (Just); eggs of the frog become unfertilizable after half an hour in water (Spallanzani); eggs of the wall-eyed pike completely lose their fertilizability after ten minutes in water (Reighard). Usually fertilization capacity begins to fall off in one or two hours after eggs are laid in most marine animals, though in some, as in the sea-urchin, it may persist much longer.

(*c*) Once fertilized eggs do not fertilize again, nor do parts of such eggs freed of the fertilization membrane. It should therefore be impossible to superimpose parthenogenesis and fertilization; and the studies of Mr. C. R. Moore, one of my students (not yet published), show this to be the case. Apparent superposition appears in all cases to be due to incomplete reactions, which cease and may be subsequently resumed. The fertilization reaction appears to be irreversible; and the appearance of reversal in parthenogenesis may be referred, like superposition of fertilization on parthenogenesis, to incompleteness of the initial reaction.

Specificity is an outstanding feature of the fertilization reaction, the significance of which is not weakened by any hybridization experiments. We need not stop to define the limits nor the consequences of hybridization in order to justify the assertion that no theory of fertilization which fails to include the factor of specificity as one of the prime elements can be true.

The fundamental character of specificity is illuminated by the phenomena of self-sterility; in species where this occurs the eggs and sperm of the same individual are sterile *inter se*, though fertile with those of all other individuals. This has led some botanists to the conception of individual stuffs; but Correns's experimental analysis led him to the conclusion that the specific factor is not an individual stuff, but a definite combination of stuffs for each individual. The combination arises always with the individual, and disappears with it. An extension of the principle of self-sterility is found in that mutant of fruit flies discovered by Morgan in which the males and females are fertile with other mutants, but sterile *inter se*. The only biological parallel of such phenomena is found in the individual blood composition revealed by serological studies. That there is a common factor in species and individual specificity studies no one who has studied both sets of phenomena can doubt.

A consistent theory of fertilization must take account of all these phenomena, not only the internal factors of maturity of germ-cells and the specificity of their reactions, but also the external factors that favor or inhibit the reaction. I have attempted to show in a series of papers that the fertilizable condition of the egg depends upon the presence of a specific substance which is produced at the time of rupture of the germinal vesicle and which disappears completely after fertilization.

If this substance be present in the egg in adequate amount, the egg can be fertilized, otherwise not. It may be obtained in solution in the sea-water and recognized by its capacity for agglutinating sperm suspensions of the same species, in some cases at least. If it is thus possible to associate the fertilizable condition of the ovum with a definite substance, we have a base from which an analysis of fertilization can be made.

If the existence of such a substance be admitted, it must operate either by activating some substance in the spermatozoon, which is to be regarded as the effective agent in subsequent changes, or we must regard it as the effective agent which is transformed from an inactive to an active state by some substance in the spermatozoon. If we take the first alternative, we have no explanation of parthenogenesis, whereas if we regard the egg substance as the active agent, the explanation of parthenogenesis proceeds along the same lines as that of fertilization. Moreover, I have been able to show by an analysis of the phenomenon of blood inhibition of fertilization, that the first point of view is untenable.

This substance may therefore be called the fertilizing substance, or fertilizin. By its reaction it is shown to be a colloidal substance, not giving the usual protein tests, and exhibiting some of the properties of a ferment as shown by Richards and Woodward. Fertilization would thus be a three-body reaction between the sperm-receptors, fertilizin and egg-receptors linked in line; and it is possible to show that inhibiting agencies may operate at the various linkages of such a reaction. In its reaction with the sperm the fertilizin of different species exhibits a certain degree of specificity, which should be more fully studied, but which has been partly explored by Jacques Loeb and myself.

This form of hypothesis takes into account the internal factors both of maturity of the germ-cells and their specificity; it is also adapted to explain the environmental conditions of fertilization extremely well; and it is consistent with the results of parthenogenesis, and the known relations of parthenogenesis and fertilization to the permeable or impermeable conditions of the egg-membrane.

I believe that I speak for all naturalists when I express my admiration for the advances in the conception of the cell due to the labors of many physiologists. But those of us who deal with the more complex phenomena of cell-life as shown in fertilization, in the behavior of chromosomes, and in the phenomena of heredity, feel that no advance in our comprehension of the cell-membrane, of the relation of cell-activity to electrolytes, nor of the chemical analysis of triturated cells, will lead to a fundamental comprehension of these phenomena. There is a great gap in our knowledge of cellular physiology, the significance of which is not generally appreciated. We know nothing except what our microscopes show us, of the reactions of the colloidal substances of the living cells; and all hope of a physico-chemical analysis of cell activities is premature until the gap is filled in.

The main physiological problems of fertilization are still before us; all the work up to the present has merely prepared the way for their solution. Fertilization is the knot in the webs of successive generations which must be untied before we can trace the strands from generation to generation. The task bespeaks all that we know, or may hope to know, of cellular physiology. As in all times of the history of the subject our vision is limited by our general biological conceptions, and the problem will move forward as our general knowledge of

cell-life progresses; and it will aid in its turn in the general advance.

We have followed the history of the problem of fertilization from the metaphysical stage through the morphological stage into the physiological stage, and within sight of the physico-chemical stage. Possibly the results seem slight as a record of 265 years of continuous study of a single biological problem. But we read the history of science very superficially indeed if we fail to realize the constant interdependence of all scientific thought. There has probably been no time in the history of our particular subject when a greater amount of work on its problems would have caused a much more rapid advance. Scientific discovery is a truly epigenetic process in which the germs of thought develop in the total environment of knowledge. Investigation of particular problems can not be accelerated beyond well-defined limits; progress in each depends on the movement of the whole of science.

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THE WORK AND OPPORTUNITIES OF A DEPARTMENT OF RESEARCH MEDICINE IN THE UNIVERSITY[1]

IF we analyze the discussions of present-day problems of medical education we find that an important if not the ultimate object of any particular plan is greater opportunity for research. This we find in the argument of those who support the plan of the full-time teacher, the plan that the university should own its hospital or control one by close affiliation, and also it is evident in all plans for greater endowment. Increased facilities for research and an augmentation of the number of men engaged in research, or combining research with teaching, would ensure, it is contended, not only important progress in the science of medicine, but also a higher development of both medical teaching and medical practise. To what extent this increased interest in research is due to the popularization of medicine through the practical application of discoveries in the fields of bacteriology and protozoology and to what extent to a dissatisfaction with time-honored methods in medical education, it is difficult to say. Both undoubtedly have had some influence but they alone can not explain the rapidly increasing number of experiments in medical education which have for their avowed object the stimulation of medical research in school and hospital. As the most important of such experiments I need only remind you of the so-called "full time" scheme at Johns Hopkins Medical School fostered by the General Education Board, the affiliation between Columbia University and the Presbyterian Hospital of New York City, the development in Chicago of the Otho S. A. Sprague Institute which, without buildings of its own, utilizes for purposes of research in medicine the already existing laboratories and hospitals of that city, and more recently in San Francisco in connection with the University of California, the establishment of a well-endowed department for general research in medicine. On a smaller scale we find the establishment, definitely within the university, of separate departments for the investigation of tropical diseases, of cancer, of tuberculosis, of chronic diseases, or of departments devoted less specifically to experimental medicine, comparative pathology, comparative physiology and the like. As all such foundations must be considered for a time at

[1] Address of the vice-president and chairman of Section of Physiology and Experimental Medicine of the American Association for the Advancement of Science, Columbus, January 1, 1916.

least, as experiments in medical education and research, and as the increase of endowment for the better type of medical effort will naturally depend to some extent upon the efforts, successful or otherwise, of the foundations already in existence, it seems advisable that those responsible for the expenditure of research funds should from time to time report upon their efforts —both useful and futile—in order to guide those giving or receiving funds for investigation in medicine. It is for this reason that I present to you, to-day, the experience of a small university research department for the management of which I have been responsible during the past five years. It is not always comfortable to talk about one's own work and efforts and I realize that I may be criticized for bringing myself and my department into the limelight in this way and particularly on this occasion, but I am satisfied from the number of inquiries I receive about the plan and scope of our work that there is a general desire on the part not only of medical faculties and university trustees, but also of individuals who wish to aid and foster research in medicine, to know more about the experience of foundations already established. For this reason, despite possible criticism, I present the general facts concerning some of the phases of the work of the John Herr Musser Department of Research Medicine of the University of Pennsylvania during the past five years.[2]

This department was endowed in 1909 under a deed of gift which provided for the establishment of a chair of research medicine in a department of similar name.[3]

[2] September 1, 1910, to August 31, 1915.

[3] In 1912 after the death of John Herr Musser, professor of clinical medicine in the university, and at the request of the original donor, the name of the department was changed to The John Herr Musser Department of Research Medicine.

Some of the important conditions contained in this deed of gift which have necessarily determined the work of the department are as follows:

1. That the department concern itself especially with the study of chronic diseases[4] by laboratory methods and with the aid when necessary of the wards of the university hospital.

2. That the professor of research medicine devote his entire time to the conduct of the department, his duties as a teacher being limited to not less than fifteen lectures or demonstrations on the work of the department to be given to students of medicine of the University of Pennsylvania.

3. That the facilities of the department be open to members of other departments of the university and to such students and practitioners as might be considered capable of conducting research work.

4. That the income of the endowment be applicable to the purposes of the department of research medicine and in and about no other department of the University of Pennsylvania or otherwise.

In brief the conditions of the endowment established a department for the study of chronic diseases, reduced the teaching duties of the staff to a minimum and provided that opportunities for research should be given to those desiring such work and that the income could not be used to eke out the expenses of existing departments. The qualifying statements, however, in regard to each of these conditions allowed considerable latitude of interpretation, both as to scope of work and relations to other departments. The work of the department, as determined by the various conditions stated, may be considered under the following heads:

[4] Some diseases were specifically mentioned, as, for example, gout, rheumatism and nephritis.

1. Investigation of the problems of certain chronic diseases.

2. Cooperative efforts with other departments, particularly the department of medicine.

3. Special elective courses of instruction for medical students, and

4. Opportunities for research offered to physicians and others.

These four lines of effort have been the chief object of the department and upon the success of these must rest opinion concerning the value of such a department to the medical school or the community.

1. INVESTIGATION

From the point of view of the investigator the field of the chronic diseases is the most difficult of approach in the entire territory of medicine and it is for this reason that our exact knowledge of these diseases progresses so slowly. The very slight knowledge we have concerning their etiology, the insidious nature of their onset, their slow progress, the frequent involvement of several organs in a general degenerative process, and the difficulty of reproducing pure types of chronic lesions experimentally, render impossible the brilliant achievements which have characterized the attack on the acute infectious diseases by the methods of bacteriology and immunology. Progress must depend on the slower methods of physiology and chemistry as used in experimental and clinical studies. The immediate problem in a given disease is to understand the gradual and progressive changes in physiology which a particular type of organic lesion produces rather than to discover its exact etiology. Naturally etiology and of course therapeusis, looking to amelioration of a chronic diseased condition, are the ultimate objects of researches in this field, but at present the best form of attack seems to be that designed to explain pathological physiology and especially the physiology or chemistry of the characteristic crises and complications, as, for example, the edema, uremia and hypertension of nephritis, the acidosis and coma of diabetes, the exacerbations of gout and so forth. The investigation of individuals, the subjects of chronic disease, by means of metabolism studies, functional tests and instruments of precision, as those applied to the cardio-vascular system, must constitute an important phase of work in this field. This must, necessarily, be supplemented by experiments on animals which have for their object the reproduction of lesions chronic in nature which may then be studied by the methods of physiology and chemistry, or, if this is not always possible, by the reproduction of isolated phenomena, or analogous symptoms or complications. Chronic disease and its phenomena can not always be imitated perfectly by experiment, but the imperfect experiment may nevertheless throw some light on the phenomena of a particular disease. Finally, a department devoted to this field of disease must be prepared to test out new functional and other tests and to apply immediately the discoveries of physics, physiology and chemistry to both the experimental and clinical study of chronic disease.

Whether or not this plan of approaching the study of the chronic diseases is the best that could be conceived, it remains the plan adopted by the department under consideration. The principal lines of investigation which have been followed during the past five years have been those concerning (1) diseases of the kidney and (2) the spleen in relation to anemia and hemolytic jaundice. The first of these studies was undertaken largely on account of the great importance of nephritis as the common dis-

ease of advancing life and so frequently responsible for the final exitus and partly because it was one of the diseases for the study of which the department was founded.[5] The studies of the spleen were inaugurated on account of the almost total lack of knowledge concerning the function of this organ, the apparent relation it has to certain hemolytic anemias, and the improvement in the latter which follows the removal of the spleen. An analysis of the publications of the department during the five years of its existence shows that nineteen are more or less directly concerned with the study of diseases of the kidney and twenty-four equally so with problems concerning the spleen. Of these about one eighth are comprehensive metabolic or other studies of patients—while the larger number were based on experimental observations on animals. Other investigations concerned themselves with anaphylactic shock, the depressor substance of various tissues and fluids, the coagulation of the blood, the cerebrospinal fluid, the utilization of parenterally introduced serum, diseases of the heart, and the toxemias of pregnancy. As to the ultimate value of this work, we naturally offer no opinion. This brief summary is presented merely to indicate the general character of the research work of the department.

Another group of fourteen publications presented the results of the study of various new functional tests and methods of diagnosis. These include such subjects as the phthalein test for kidney function, Abderhalden's test for pregnancy, Folin's methods for non-protein nitrogen in the blood, the tetrachlorphthalein test for liver function, a critical study of Crehore's micrograph for recording heart sounds, and the technique of the Eck fistula operation with regard to its possible application to human surgery.

This testing of new methods, while not to be dignified as original investigation, we have considered nevertheless to be an important part of our work. It is well known that the busy hospital laboratory can not take up at once every new diagnostic aid that is announced. If the new method involves a simple technique and is easy of application it may gain wide use at once; but if further observation and experiment is necessary and especially if it demands animal experimentation, or new laboratory equipment, the average hospital waits until further trial in the laboratories of the medical sciences demonstrates its value and thus finally forces its practical application. We have felt that we are justified in giving a part of our time and resources to work of this character in order to reduce the waiting period which usually follows an announcement of a new procedure, applicable to the study of chronic disease. Incidentally the educational value to the department staff is a matter of no small importance, for its members at once become familiar with the technique of the new procedure, and such as engage also in hospital work or clinical teaching can at once put the method into practical use or instruct medical students and others concerning its value.

2. Cooperation with other departments

It is not the usual cooperation between departments that I wish to describe at this time. Every department desires from time to time the assistance, in connection with the solution of its problems, of the skill or equipment of other departments and this has naturally been our experience in connection with the widely varying methods of studying chronic diseases. We have found it necessary to call on the department of

[5] The deed of gift referred specifically to diseases of the kidney.

surgical research for the aid of its special skill in peculiarly difficult operative procedures, on the department of pathology for cooperation in problems demanding the methods of immunology and frequently on the department of physiological chemistry for cooperative assistance in technical procedure. On the other hand, we have given assistance in the solution of their problems to the departments of medicine, neurology, surgery and obstetrics. In the case of each of the departments named the cooperation has been successful inasmuch as the combined efforts at investigation have resulted in the publication of material of benefit to the departments interested. It has been our experience, moreover, that the presence of departments for research[6] stimulates among the workers in various other branches much discussion of borderline problems, with the result that the presence of one or more groups of men, giving their time entirely to research, encourages doubtful or difficult ventures in investigation that the teacher with his many duties and limited time for research would not attempt without the assistance of a department interested in research only. This is particularly true of the average busy clinical teacher whose hazy views on some theory or problem occasionally suggest a workable basis for orientative experimentation. With such views, in that they do not always concretely set the problem, the workers in the fundamental sciences of medicine are usually somewhat impatient. When, however, a department for the general investigation of disease exists, it can afford, in the hope of securing better cooperation with the clinical side of medicine, to sift and analyze such suggestions, and if a possibility of profitable investigation, or of definitely settling a moot point, is seen, it is justified in utilizing a certain amount of its time and funds in thus assisting the clinical department. And if in so doing it can persuade members of these departments to actively cooperate in the solution of the problems under consideration, and thus stimulate the spirit of exact investigation it is doing as much, if not more, for research and the development of clinical medicine than it would by restricting its efforts to the hard and fast lines of fundamental problems.

This cooperative work with other departments, valuable as it is, is, however, as a rule more or less incidental and without definite responsibility on the part of either party concerned. It does not represent sustained cooperative effort, but rather the coming together of two departments when mutual need arises. We have, however, with one department, that of the theory and practice of medicine, developed a community of interest and definitely cooperative effort which we regard as a most important experiment in medical education. Three years ago an agreement was entered into with the professor of medicine (Dr. Alfred Stengel), and largely at his suggestion, by which it was provided that the two associates most intimately concerned with him in the teaching of students and the care of patients in the university hospital, should give half their time to investigation in the department of research medicine. In other words, two men intimately connected with the fundamental instruction in clinical medicine were to devote their mornings to the teaching of students and the care of patients and their afternoons to fundamental research in a laboratory independent of the hospital. In the absence of the "full time" plan in the clinical departments of the school this seemed an experiment with "full time"

[6] This refers not only to the department under discussion, but as well to the department of surgical research under the direction of Dr. J. E. Sweet.

assistants well worth trying. It should be stated that this arrangement was not due to a lack of opportunity for research laboratory work in the hospital. The university hospital has two spacious and well-equipped laboratories, one in the hospital proper for the usual routine examinations and the other, The William Pepper Laboratory of Clinical Medicine, in a separate building, with an independent endowment and a large staff, engaged in the various research problems arising in connection with clinical observation in the wards. The cooperation with the department of research medicine, which has its laboratory in the medical school building, was for the purpose of enlarging the opportunities of the department of medicine and the department of research medicine by bringing the latter into closer contact with the problems of the wards, and allowing workers in the former department the utilization of the methods of the fundamental sciences in the solution of their problems and the broadening of their training. During the three years this arrangement has been in operation the results have been most gratifying and the arrangement has been of advantage to both departments. The research work of the two men concerned has been in part the study of patients under their care by the detailed methods of metabolic investigation and the use of functional tests, in part experimental work on animals in connection with fundamental problems, and in part the careful testing out of new methods of possible clinical application. Fully a third of the researches of the department completed during the past three years have been published under their names, either as independent authors or in collaboration with other members of the staff. On the side of productive research this is for them a most creditable showing; on the other side, that of their development as clinical teachers, there is abundant evidence that they have found this experience of great value. But for the university there is also something gained. Men desiring to devote themselves to a career as teachers of medicine can by this cooperation gain the proper balance between teaching, research and routine ward work without one phase suffering at the expense of the other. They can keep at all times in touch with each field of activity, and when the time comes that a man is overwhelmed by the lure of the clinic and finds that he must curtail the time given to fundamental research, and feels obliged to limit his investigations to the hospital laboratory, the university has the assurance that his fundamental laboratory training has been satisfactory. On the other hand, it is to be hoped that such a system will occasionally stimulate and hold the rarer type of clinical mind which finds its greatest satisfaction in the solution of the more difficult fundamental problems of medicine rather than in the practical applications of the clinical laboratory. Clinical medicine needs most men who would rather blaze a new path than clear the trail of those who have gone before. It is only through conscientious effort in the fundamental investigation of disease that such can be developed. To assist in developing men of this type is a function of the research laboratory in the university but, falling short of this, it can do what is perhaps only second in importance—cultivate proper ideals in its younger clinical teachers.

3. Elective Courses

The requirement, in the deed of gift, that the department should engage in teaching to the extent of not less than fifteen lectures or demonstrations in each year has been met by offering special elective courses, dealing with the experimental side of medi-

cine, and largely demonstrative in nature. It was the intent of the founder of the department, apparently, that the lectures or demonstrations offered should be given to an entire class. This plan was not carried out, partly because it would duplicate work already given in a systematic way by other departments and partly because it seemed unwise to add another set of didactic lectures to an already overcrowded curriculum. An alternate plan was therefore adopted of a series of elective demonstrations so arranged as to supplement the didactic and clinical teaching in other departments and to illustrate by experimental procedures, in a more or less intensive way, the physiology, chemistry and pathology of various organs or groups of organs. With a desire to determine the best system for such teaching, and also to find out what type of work and instruction appealed most to the student of medicine, the subject matter and method of this instruction has been changed from year to year. As our efforts in this regard are of some interest they will be briefly summarized. During the first year a comprehensive series of demonstrations in experimental pathology was given for the benefit of the class (second year) in pathology. This was offered twice a week during a period of fourteen weeks, half the class attending, if they desired, one demonstration each week. The subjects covered were degeneration and necrosis, inflammation and repair, blood destruction and jaundice, thrombosis embolism and infarction, experimental lesions of the heart, lungs, stomach, intestines, liver, pancreas, and kidney, the problems of infection and immunity, of shock and hemorrhage and the physiology of the ductless glands.[7] As far as possible the gross and microscopic lesions of disease in man were correlated with experimental lesions and the relations to clinical medicine emphasized. Physiological methods of graphic registration were employed whenever possible; changes in the urine and other secretions demonstrated; and the methods of chemical examination shown. Furthermore, in the exercises on the heart and lungs the work was done in cooperation with the instructor in physical diagnosis.

In the following three years this course was not offered in its entirety. Thus one year a group of ten students (fourth-year class) studied with great thoroughness the normal and pathological physiology of the cardio-vascular system, and in the following year the same course was given as a demonstration course and in less detail to the entire third-year class, divided into sections for this purpose. In still another year the problems of hepatic and renal and pancreatic disease were taken up by small groups of men from the fourth-year class.

At the end of four years of such concentrated experimental work we were impressed by the fact that although the student had gained a better insight into the problems of pathological physiology and therefore of disease processes, the time given to the various experimental procedures left little or no time, in our short two-hour periods, for the discussion of theories and the relation of new facts to old conceptions. And even with the constant presence at all these exercises of the two clinical associates, to whom I have previously referred, whose interest led them to emphasize matters of clinical importance, we felt that a thorough correlation of experimental procedure and clinical observation was not always attained. In the fifth year, therefore, we tried the experiment of a seminar for the discussion of the various problems peculiar to certain groups of disease. In this sem-

[7] Pearce, R. M., "The Teaching of Experimental Pathology and Pathological Physiology to Large Classes," *J. H. H. Bull.*, 1911, XXII., 1.

inar were united the chairs of medicine (Dr. Alfred Stengel), pharmacology (Dr. A. N. Richards), physiological chemistry (Dr. A. E. Taylor) and research medicine with their respective staffs and the seminar was thrown open to students of the fourth-year class as an elective. The medical clinic room of the hospital was used for these exercises in order that lantern demonstrations and the exhibition of patients might be possible. All other demonstrations were barred in order to have plenty of time for discussion. The first trimester started auspiciously with the discussion of diabetes and a sufficient number of students in attendance to guarantee, apparently, the success of the venture. But no student elected the course for the second and third trimesters devoted respectively to renal disease and diseases of the ductless glands. In brief, from the point of view of interesting the medical student, the seminar was a dismal failure. For the teaching and research staffs represented, the exchange of views was very profitable and despite the absence of students the seminar was continued through the year. It is perhaps needless to say that the students lost interest because of the many detailed discussions of opposing and oftentimes irreconcilable views which led the disputants away from the fundamental basis of accepted facts. Perhaps also the fact that the students could take no part in the exercises, except to ask questions, had something to do with their lack of interest.

We have, therefore, abandoned the seminar as an aid to discussion—perhaps it smacks too much of the didactic lecture, anyway—and have this year returned to the plan of offering to small groups of men three short, elective experimental courses dealing respectively with the cardio-vascular system, the liver and bile passages and the chronic degenerative diseases.

I have gone into these experiments in elective teaching in some detail because not only do I feel it is a very important part of our work, but also because I am convinced that in every school the men of the fourth year should have some means of reviewing in a practical way the knowledge they have obtained of one or more of the systems of the body. No better method exists, I believe, than the experimental course with its demonstrations of pathological physiology and chemistry, the necessary review of physiology, pathology and pharmacology and the obvious applications to clinical medicine. In short, such courses help to bring physiology into relation with morphology and to fill the gap which exists between pathological anatomy, on the one hand, and the clinic on the other. It is perhaps peculiarly the function of a university research laboratory[8] to develop such courses, and I consider our efforts in this direction to be a very important part of our work during the past five years.

4. Research by Students and Practitioners

The fourth of the important objects of the department has been to furnish opportunity for investigation, as stated in the original deed of gift, "to properly trained students and practitioners" of medicine. In this, in so far as the student is concerned, we have not been successful. This is, however, not the fault of the department, which has always been ready to encourage research by the medical student; nor, on the other hand, is it the fault of the students, many of whom have attempted to find time for a moderate amount of research work.

[8] In connection with our practical working out of these courses no claim for originality is implied. The general plan here outlined is largely that used several years ago in the department of pathology of the Johns Hopkins School by Professor W. G. MacCallum.

The failure is due to the demands of an overcrowded inflexible curriculum and an inadequate elective system. During only one trimester, a period of a little more than ten weeks, in the fourth year, has the undergraduate any freedom in the choice of work and in this period the total of hours that may be given to purely elective work is so small that sustained investigative work is impossible. A few enthusiastic students have occasionally attempted to utilize Saturday afternoons and odd hours during the week, but with, as was to be expected, no very definite results. As a matter of fact, during the five years the department has been in existence only one piece of work by students, deserving of publication, has been completed, and this represented student labors during a summer vacation period. The summer climate of Philadelphia, however, is not conducive to close laboratory work and students desiring medical work in the summer are inclined to seek fields demanding less arduous efforts than those of the research laboratory.

Our experience, then, has demonstrated the futility, in the absence of a liberal elective system, of attempting to interest students in independent investigation. Our present attitude is to recommend to those seeking such that they take the special elective courses which we have already described. These at least give a first-hand knowledge of experimental methods and some idea of the problems of medicine, and this is about all that can be accomplished in the small amount of time our students have for elective work.

The situation in regard to the practitioner of medicine is quite different. During the five-year period under analysis, about fifteen practitioners have entered the department for the purpose of carrying on definite investigative work, and of these, nine, either working alone or in collaboration with members of the regular staff, carried to completion a total of fifteen researches. In part these researches had a close relation to clinical methods and problems, but in a number of instances they were fundamental investigations in experimental pathology. All these workers have expressed the liveliest satisfaction at the opportunity afforded them and in many instances have continued an interest in the research side of medicine. These were, for the most part, younger men, with their hospital interneship back of them, who were starting the practise of medicine and wished to divide their spare time between dispensary and research work, or, as in some instances, to devote it entirely to investigative work. We have felt that a department for research in medicine could use its resources in no better way than to encourage such aspirations and for this reason every effort has been made to guarantee to these men accomplishment without undue loss of time or effort in petty routine work. Naturally such men do not remain for any great length of time[9] because of the demands of practise, hospital, dispensary and other clinical work, but if they carry into the latter the spirit of the investigator and utilize the hospital laboratory in the study of clinical problems, the time and effort given in their behalf by the research laboratory is not entirely lost. If the progress of medicine depends, as we like to think it does, upon the spirit of investigation, young men entering upon the practise of medicine should devote a part of the post-hospital period to methods of exact observation and experiment, and if a university possesses a department of research in medicine, one of its first duties

[9] One man remained with us four years and another two years: the others averaged about six months each.

is to offer to recent graduates who have enough time at their disposal, facilities for such work. For its ultimate success, however, such a policy must have the sympathy of the clinical teachers. If the latter discourage the spirit of research, and do not themselves engage in investigation, and especially if they urge that the younger men enter immediately, and to the full extent of their time, into distinctly clinical work, the research department need not expect many voluntary workers, and might as well plan its activities on the basis of its permanent full-time staff. If, on the other hand, the clinical atmosphere is stimulating and progressive, the research laboratory is perhaps doing its greatest good in providing for the men who wish to combine clinical observation with experimentation in the laboratory.

In this brief discussion of the main phases of the development of the department under discussion I have thus far omitted all reference to the questions which are frequently asked concerning such a department. Is not a department in the university for research only an anomaly? Should not the teacher be an investigator and the investigator a teacher? Would it not be better instead of a department for research only, to divide an endowment for research among existing teaching departments? These and many similar questions have often been put to me during the past five years and I have always answered that teaching and investigation, in my opinion, should go hand in hand, and that if adequate endowment could be procured to place teaching and research in every department of the medical school on a basis which would ensure adequate results, there would be no need for a separate department of research. Unfortunately no school possesses such endowment and probably will not for some time to come. In the meantime, it is evident that there is a tendency on the part of those wishing to advance the knowledge of certain diseases, or groups of disease, to offer to universities funds for the study of such. For the most part these funds do not represent large endowments, but sums which average two or three hundred thousand dollars and are for this reason given to institutions, as universities, which already have the buildings in which such concrete department may be housed, thus obviating the necessity of spending the income or a part of the principal for a new building. Likewise it is usually stipulated that the money is to be used for research and not for teaching. The object of this provision naturally is to prevent the diversion of funds to purposes other than those for which the gift was intended. Such gifts obviously intended for the more or less concentrated study of one disease or a group of disease can do little more than support a chair with one or two assistants or fellows, if much is to be left for diener services and expenses of equipment and maintenance. Its work at the most must be modest in comparison with our larger well-endowed non-university research institutions. But despite these restrictions as to scope, purpose and field no university can refuse a gift which means an added effort for the advancement of medicine. Gifts similar in character, and, it is to be hoped, larger in amount, may come to any medical school prepared to take up such work, and their trustees can not refuse them on the ground that they do not believe in departments for research only and prefer to wait for endowment which may be used to combine research with teaching. They will in the future, as in the past, accept them, in the hope that a research department will find not only a field for independent work, but as well many opportunities to cooperate with and to aid and complement other de-

partments interested primarily in teaching.

To emphasize some of these possibilities and opportunities, as exemplified in our department at Pennsylvania during the last five years, in the hope that our experience may be of benefit to other universities, is the principal object of this exposition.

RICHARD M. PEARCE
UNIVERSITY OF PENNSYLVANIA

SCIENTIFIC NOTES AND NEWS

DR. EUGENE WOLDEMAR HILGARD, professor of agriculture in the University of California from 1875 until his retirement in 1904, distinguished for his contributions to agricultural chemistry and geology, died on January 8, in his eighty-fourth year.

THE American Association for the Advancement of Science held a special meeting in Washington on January 3 and 4, in honor of the Pan-American Congress. On the evening of January 3 Dr. R. S. Woodward, president of the Carnegie Institution, presided, and Dr. W. W. Campbell, president of the American Association, delivered an illustrated address on the "Evolution of the Stars." On January 4 two sessions were held at the new National Museum when programs were presented relating mainly to the natural history of South America.

THE Italian government has placed the zoological station at Naples under the control of a royal commission, of which F. Sav. Monticelli, professor of zoology in the University of Naples, is president. The commission announces that it will furnish means to continue the work of the station, and engagements entered into in regard to tables for research.

DR. REID HUNT, of the Harvard Medical School, has been elected president of the American Society for Pharmacology and Experimental Therapeutics.

DR. SAMUEL G. DIXON has been elected president of the Academy of Natural Sciences, Philadelphia, for the twenty-first time and executive curator for the twenty-fifth time.

ROBERT BRADFORD MARSHALL, chief geographer of the United States Geological Survey, has been appointed superintendent of national parks.

DR. JOHN S. BILLINGS, JR., has been appointed deputy health commissioner of New York.

MR. BURIAN, the Austrian premier, is reported to have suggested through a neutral ambassador that Dr. Robert Bárány, the Viennese aurist and winner of the Nobel prize in medicine, now a prisoner in Russia, be exchanged for a Russian prisoner held in Austria.

DR. ALFRED IRVING LUDLOW, professor of surgery and surgical pathology, Seoul Medical College, Korea, will sail for the Orient to resume his duties on January 8, 1916.

PROFESSOR GEORGE NEIL STEWART, director of the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University, has returned from abroad.

THE magnetic survey vessel, the *Carnegie*, at present under the command of J. P. Ault, of the Department of Terrestrial Magnetism, arrived at Port Lyttelton, New Zealand, on November 3, after a successful continuous trip of ninety days from Dutch Harbor, Alaska. Leaving Port Lyttelton on December 5, the *Carnegie* is now engaged on the accomplishment of the circumnavigation of the region between the parallels 50° and 60° south, where almost no magnetic data have been secured during the past 75 years.

A BIOLOGICAL expedition to the island of Santo Domingo will be undertaken next fall by Professor J. G. Needham, of the department of entomology in the college of agriculture, Cornell University. He will be accompanied by his son, J. T. Needham, '18, and by Ludlow Griscom and K. P. Schmidt, both assistants in his department.

PROFESSOR C. P. BERKEY, of the department of geology of Columbia University, has just completed a series of investigations of the geology of New York City. He has mapped out a scheme to save borings or explorations for any project in the city, such as aqueducts,

tunnels or building foundations. Professor Berkey has constructed a map of the city on which will be plotted the findings of such borings to be used for future reference. In this way the substrata of the entire city will in time be plotted on the map and engineers working on any project will be spared the trouble and expense of new determinations.

Before the Geographical Society of Chicago on January 14 there was an illustrated lecture by Mr. Anthony Fiala entitled "Through the Brazilian Jungles with Colonel Roosevelt"; on January 28, Professor William I. Thomas, of the University of Chicago, will lecture on "The Comparative Mental and Moral Worth of Races."

Dr. Frank G. Speck, assistant professor of anthropology in the University of Pennsylvania, lectured before the Geographical Society of Philadelphia on January 14 on "Hunting Territories and Game Rights of the Tribes of the Lower St. Lawrence."

At the 221st meeting of the Elisha Mitchell Scientific Society, held in the Chemistry Hall of the University of North Carolina on December 14, the program consisted of an address on "Some Phenomena of Fluid Motion and the Curved Flight of a Baseball," by Dr. W. S. Franklin, formerly professor of physics, Lehigh University. On December 20 Professor Franklin delivered a lecture at the laboratory of the Department of Terrestrial Magnetism at Washington, entitled, "On the Limitations of One-to-one Correspondences in Physics."

Dr. L. A. Bauer gave an illustrated address at the Carnegie Institution of Washington on December 9 on "Our Earth a Great Magnet."

Dr. J. J. Tauberhaus, associate plant pathologist of the Delaware Experiment Station, will deliver the John Lewis Russell lecture before the Massachusetts Horticultural Society on March 27, on "Diseases of Sweet Peas."

At the annual meeting of the trustees of the Adirondack Cottage Sanatorium, December 21, Dr. Walter B. James, New York City, was elected president; Dr. Edward R. Baldwin, Saranac Lake, vice-president; Mr. George S. Brewster, secretary-treasurer, and Dr. Frederick H. C. Heise, Trudeau, resident physician. The trustees adopted a resolution paying tribute to the memory of Dr. Edward L. Trudeau and directing that this tribute be spread on the records of the meeting.

The *Journal* of the American Medical Association states that the *Presse Médicale* gives an illustration of the large tablet to be erected under the arcade of the great staircase of the medical department of the University of Paris. In October the design, already in place, contained the names of six members of the faculty, victims of the war (Galland, Legrand, Moog, Pelissier, Schrameck and Reymond—the latter the aviator). There are also inscribed the names of forty-seven students, and of twenty-six former graduates of the institution. Landouzy comments on this total of seventy-nine medical victims that the new methods of warfare have incredibly increased the dangers and privations of the medical men with the army. They keep right with the men in the trenches and toil on while others sleep.

Francis Marion Webster, of the Bureau of Entomology, died on January 3 in Columbus, O., at the age of sixty-six years.

Dr. James Clarke White, adjunct professor of chemistry in the Harvard Medical School from 1866 to 1871, and professor of dermatology from 1871 until his retirement as professor emeritus in 1902, died on January 6, in his eighty-third year.

Professor Robert James Davidson, since 1891 professor of chemistry at the Virginia Polytechnic Institute and dean of the scientific department, died suddenly on December 19, in his fifty-third year.

Dr. Walter L. Capshaw, for seven years professor of anatomy at the University of Oklahoma, died suddenly of pneumonia at his home in Norman on Christmas morning. He was a graduate of St. Louis University and intended studying in one of the eastern schools while on sabbatic leave this year, but was prevented on account of ill health.

Dr. Charles Clifford Barrows, professor of gynecology at the Cornell University Med-

ical College, died on January 3, aged fifty-nine years.

DR. JOSEPH J. O'CONNELL, health officer of the port of New York, lecturer on hygiene in the New York University and lecturer on public health in the Long Island College Hospital, died on January 1, at the age of forty-nine years.

DR. W. A. BORGER, assistant director of the Pasteur Institute and vaccination service in Java, has died, aged forty years. He succumbed to laboratory infection from research on bubonic plague.

THE death of Dr. Jules Ville, professor of medical chemistry at the Faculté de Montpellier, is announced.

THE annual general meeting of The American Philosophical Society will be held on April 13, 14 and 15, 1916, beginning at 2 P.M. on Thursday, April 13.

THE sessions of the fourth annual meeting of the New York State Forestry Association will be held at Syracuse on January 21. The program has been considerably broadened and in addition to discussing forests as producers of timber there will be considered the necessity of the forests in controlling the run-off of water, the forests as a recreation place and as a home for fish and game. The Honorable Gifford Pinchot and Chief Forester Graves, of the U. S. Forest Service, have been invited to speak. The list of speakers will include also John B. Burnham, president of the New York State Fish, Game and Forest League, who will give an illustrated address on game protection and propagation, and Dean Baker, of the State College of Forestry at Syracuse, who will speak on forests and the conservation of water in the state.

THE directors of the Fenger Memorial Fund announce that $550 have been set aside for medical investigation in 1916. The money will be used to pay all or part of the salary of a worker, the work to be done under direction in an established institution, which will furnish the necessary facilities and supplies free of cost. It is desirable that the work undertaken should have a direct clinical bearing. Applications should be addressed to Dr. Ludvig Hektoen, 637 S. Wood St., Chicago.

THE *Journal* of the American Medical Association reports that President Wilson will submit to congress a plan for a system of public health hospitals to take the place of the present condition of contract care of patients and government hospital service. The first step will be to take over the meteorological research station at the summit of the Blue Ridge, Mount Weather, Va., and convert it into a hospital for sailors and other patients from the Atlantic seaboard. Within another year locations will be selected for hospitals in southern California and the southeastern part of the United States.

UNDER date of December 8, from Rome, the trustees of the Permanent Wild Life Protective Fund are informed by Frederic C. Wolcott that "the Italian Government has at last passed a law, which goes into effect on January 1, prohibiting the shooting of all song and insectivorous birds throughout Italy." If this prohibition also includes, as it is only fair to assume that it does, the netting of all such birds, then Italy has indeed carried into effect a great reform. The importance of this action to the birds and the crops of Europe is beyond computation. Hitherto the netting of song birds while on their migrations has been a widespread industry, and the deadly roccollo has each year slaughtered hundreds of thousands of the choicest song-birds of Europe for food. Both in America and in England this abuse has been severely denounced, and an American bird protector has declared that it was "a reproach to the throne of Italy." The causes which brought about this reform in Italy, in spite of the excitement of war, are as yet unknown.

THE *American Museum Journal* states that the large collection of prehistoric pottery collected by Mr. Algot Lange on the island of Marajo has been acquired by the American Museum. Marajo Island in the mouth of the Amazon River is 165 miles long by 120 wide, and belongs to Brazil. A collection of some two thousand pieces comes from Pacoval Island in Lake Aray, the source of the Aray

River. Mr. Lange described the little island of Pacoval as an archeological mine. Fragments of pottery cover the ground and everywhere the earth is mixed with pottery ranging in size from minute pieces to vessels weighing as much as twenty-five pounds. Nothing is known of the makers of this ware. Who they were or where they came from is at present a mystery, but it is hoped that a study of the unique and beautiful decorations on the pottery will afford some information on the point.

The Bureau of City Tests of the University of Cincinnati has submitted its annual report through Director E. K. Files. The report states that 1,024 samples have been examined, including coal, cement, gas, soot fall, oil, asphalt and soap. Less than one per cent. of the samples received have been rejected because of inferior material, so that the city in its purchases is enforcing a high standard of quality. New developments in the bureau are as follows: (1) Two cooperative chemical engineering students are employed in the laboratory to give supplementary tests and more complete analyses; (2) since last May, atmospheric pollution in Cincinnati has been studied. The deposits collected in various districts of the city are analyzed each month and the difference in composition of carbon, tar, acids, etc., between the street level and upper stories of buildings in the downtown districts is being worked out. This study will continue and is valuable for showing the effectiveness of smoke-prevention work. Other interesting investigations now being made are on the influence of the composition of coal on the fusibility of the ash and the causes of variation in the density of natural gas during the different seasons. The bureau is now doing work for the following departments of the city: Engineering, Sewerage, Purchasing, Street Lighting, Board of Education, University of Cincinnati, Park, Fire and Smoke Inspection Bureau.

The recognition by citizens generally that the Geological Survey is a bureau of information as well as a field service has gradually placed upon it a large burden of work as well as of responsibility. The amount of correspondence involved in performing this public duty may be indicated by the fact that approximately 50,000 letters of inquiry were handled in the different scientific branches of the survey last year. The scope of these inquiries is not less noteworthy, for they range from requests for information concerning the geology of every part of the United States or the water supply, both underground and surface, of as widely separated regions as Alaska and Florida, or for engineering data on areas in every state in the union, to inquiries regarding the natural resources of foreign countries, especially those of Central and South America. The changes in the world's trade in metals and other mineral products during the last year brought to the Geological Survey a new opportunity for special service. The inquiries concerning possible sources of this or that mineral product began early in August, and the Secretary of the Interior gave to the public an interview outlining the expected developments in the mineral industry. His statement was followed by special press bulletins issued by the survey on the more important subjects. In September, 1914, however, the demand for authoritative information had become so lively that a bulletin—"Our Mineral Reserves" was issued. In this publication the subject of the country's ability to meet the emergency demands for minerals was summarized and the survey offered to serve as an agent in bringing consumer and producer into touch with each other. This new function of acting as "central" to the mineral industry proved popular, a large volume of special correspondence developed, and a gratifying use was made of the Geological Survey's list of mineral producers and of the specific information in the possession of the federal geologists regarding practically every type of mineral deposit in the country. It is believed that this correspondence has been of material advantage to consumers and producers alike—the users of mineral products who were formerly dependent upon foreign sources of supply and the mine operators who have learned of new markets for their output.

The Department of Agriculture is taking action, through the Biological Survey and the Forest Service, to combat a serious wave of

rabies infection of wild and domestic animals that is in danger of becoming wide-spread in the far west. The fact that the extensive dissemination of the disease is taking place through the agency of coyotes makes the situation a difficult one to meet. Outbreaks of rabies among coyotes have been noted from time to time for several years in parts of Washington, Oregon and northern Idaho, and the Forest Service undertook last year to aid in bringing the disease under control by employing hunters to make war on coyotes in the National Forests of some infected localities. Since, however, the coyotes breed in the foothills and around the outskirts of the forests, a more comprehensive campaign is called for. The eradication of coyotes in sparsely settled or rough country is said to be an exceedingly difficult task. Inasmuch as these animals are always a source of considerable losses to the livestock industry of the west, congress last year provided a special fund of $125,000 to be spent by the Biological Survey for the eradication of predatory animals both in the national forests and on the public domain, and from this fund a special allotment has now been made to provide for fighting the rabies. The disease first appeared in parts of eastern Oregon and Washington and northern Idaho, in a region surrounded by natural barriers which tended to confine the outbreak. Domestic animals and human beings were bitten, and a good deal of alarm was manifested by residents of the infected districts, many of whom feared for the safety of their children on the roads to and from school. The disease is now reported as having extended into northern Nevada and northern California, whence it may easily be carried far. The Forest Service, the Biological Survey and the State Board of Health are working together to meet the situation in California. Modoc and Lassen counties have been put under quarantine by the state board, which has appointed forest rangers inspectors in Modoc County. Funds have been provided by the Biological Survey for the employment of additional men and the purchase of traps and poison. The public will be enlisted in the campaign, which will be led by the Biological Survey officials and the forest rangers.

UNIVERSITY AND EDUCATIONAL NEWS

WESTERN RESERVE UNIVERSITY has purchased twelve acres of land adjoining its present site and increasing it from 23 to 35 acres. The amount paid for the land is not made public, but the tax valuation is $230,000.

FOUR business men of Portland have contributed $25,000 toward the new buildings for the Medical Department of the University of Oregon, Portland. This makes available the $50,000 appropriated by the state. The officers of the college now propose to raise an additional $100,000.

OVER $3,500 worth of chemicals, scientific glassware and other laboratory supplies ordered by the University of Washington from Germany a year ago, but held up at Rotterdam, will shortly reach this country. The British embassy has advised government officials that importation will not be prevented any longer.

A RECENT fire is said to have caused $50,000 damage to the Havemeyer chemical laboratory of New York University.

DR. OWEN L. SHINN, professor of chemistry in the University of Pennsylvania, has been appointed director of the university summer school.

THE following new appointments have been made in the Western Reserve Medical School: Dr. J. Rogoff, formerly of the department of physiology and pharmacology, Vanderbilt Medical School, Nashville, to be instructor in experimental medicine; Dr. C. H. Fiske, formerly assistant in biological chemistry, Harvard Medical School, to be associate in biochemistry; Dr. R. W. Scott, formerly demonstrator of medicine, Western Reserve University, to be instructor in physiology.

DISCUSSION AND CORRESPONDENCE

THE DETERMINATION OF NITRATES IN SOILS

IN the June number of the *Journal of Industrial and Engineering Chemistry* appeared an interesting article by E. R. Allen, of the Ohio Agricultural Experiment Station, en-

titled, "The Determination of Nitric Nitrogen in Soils," in which several of the older methods for determining this elusive radical received extended and probably deserved criticism.

Among those receiving its full share was the aluminum reduction method proposed by the writer a little over two years ago. The title of the article proclaiming this method was, "The Aluminum Reduction Method as applied to the Determination of Nitrates in 'Alkali' Soils." It was at that time put forward by the writer, not as the best possible method that the future might develop for this purpose, but as one which, in the presence of the soluble chlorides, sulfates and carbonates abounding in the "alkali" soils of the arid west, would give far more reliable results than the phenol disulfonic acid method of Gill then commonly used in soil work. Comparisons with this latter method are given. Another reason for developing the method in question was to accurately determine nitrates in nitrification cultures in soils containing one or more of the "alkali" salts. Occasionally large amounts of nitrates are here encountered, and, as was shown, when more than twenty or twenty-five milligrams of nitrogen as nitrate are present, the colorimetric method previously mentioned is of questionable value even in the absence of "alkali."

Briefly, the criticism of the method as made by Allen is that very high amounts of soluble humus and organic matter cause incomplete reduction, the results running low.

As all soil scientists know, the "alkali" soils of California and other arid sections are *very low* in soluble organic matter commonly termed humus.[1] They vary from almost nothing to, in some few cases, 3 per cent. The average for the surface soils of California is 1.28 per cent. It was for these soils, and not for those high-humus soils of the middle west, that the aluminum reduction method was originally intended. It was satisfactorily tried out with varying amounts of the "alkali" salts singly and combined, also with soluble organic matter in the forms of glucose and soluble humus, in amounts far in excess of that ever leached from "alkali" soils with distilled water.

The writer admits that some of the statements made for the accuracy of his method were possibly too broad and far-reaching, but they were made more especially with reference to its application to "alkali" soils, as the title should suggest. The method, as proposed, has been successfully used by others in arid sections, and the author still recommends it for use under such conditions.

In conclusion the writer wishes to state that he will be the first to welcome any method for determining nitrates in soils which combines accurate and reliable results with a minimum of time expended.

Note.—Since the above was written (July last) an article entitled "The Determination of Nitrates in Soil," by R. S. Potter and R. S. Snyder[2] has appeared in which the aluminum reduction method, proposed by the writer and criticized by Allen, is shown to be far superior to the colorimetric methods even where the high humus soils of Iowa were used.

P. S. Burgess

The Experiment Station of the Sugar Planters Association, Honolulu, H. I.

[1] See "Humus and Humus-nitrogen in California Soil Columns," University of California Publication in Agricultural Science, Vol. 1, pp. 173–274, by R. H. Loughridge.

A SIMPLE METHOD FOR THE ELIMINATION OF PROTOZOA FROM MIXED CULTURES OF BACTERIA

Protozoa, particularly various flagellates and ciliates, often hamper the study of the higher bacteria in mixed cultures.

Such cultures may be readily and effectively freed from these undesired animals by centrifugalization. By this means protozoa are quickly thrown to the bottom of the tube, while the bacteria for the most part remain in suspension. If subcultures are then inoculated from the supernatant fluid they will be found entirely freed from protozoa.

Doubtless this "fractional" centrifugali-

[2] *Jour. Ind. and Eng. Chem.*, Vol. 7, No. 10, p. 863.

zation has been previously practised by other workers, but as I have never seen mention made of it, I bring it to the attention of bacteriologists.

HENRY N. JONES

SYRACUSE UNIVERSITY

SCIENTIFIC BOOKS

Cancer, Its Cause and Treatment. By L. DUNCAN BULKLEY, M.D. New York, Paul B. Hoeber, 1915.

Various writers, especially Williams in his book on the natural history of cancer, have attributed great significance to the mode of life, especially to the diet as a factor in the origin of cancer. He pointed out that cancer is much less frequent among races which are vegetarian. Dr. Bulkley defends in his lectures a similar thesis: cancer (both carcinoma and sarcoma) is due to errors in the mode of living, not only to an overindulgence in a meat diet, leading to the production of nitrogenous poisons which are not properly eliminated, but also to the consumption of tea, coffee and alcohol. In consequence the saliva becomes acid, increased putrefaction takes place in the large intestines, the glands with internal secretion do not functionate well, the kidneys cease to secrete sufficiently, and the body fluids which bathe the cells become abnormal (especially too acid), thus stimulating certain embryologically aberrant cells to cancerous growth. Other factors, like traumatism play only a secondary part. In support of his views the author cites statistical data which show that frequency of cancer is greatest where so-called civilization has farthest advanced, that the increase in cancer which is observed everywhere is real and caused by a corresponding increase in false living; that experimentally it has been shown that the growth of (transplanted) cancer in animals can be influenced through certain diets; that clinically, cancer has been cured by the author in a considerable number of cases by instituting an appropriate mode of living aided by the use of drugs stimulating elimination of waste products and certain other procedures.

It is impossible to enter into a detailed critical analysis of this position. We must, however, point out that throughout the author's argumentation no sharp distinction is made between fact and hypothesis. Facts opposed to his thesis are ignored or minimized in their importance. We may mention a few objections which might be raised: We do not know at the present time how much the mode of living, external conditions and hereditary factors influence the distribution of cancer among different people. We know that constant irritation of certain kinds may produce cancer in a large percentage of persons, provided the irritation is active over a sufficiently long period of time. We have shown that on the same mouse farm in Granby, under the same vegetarian diet, certain strains of mice are almost exempt from cancer, while in other strains, as a result of hereditary peculiarities, the large majority of all females become affected by cancer of the breast. It is now known that the presence of embryologically displaced cell nests is not necessary for the development of cancer.

There occur in addition to the main arguments not infrequently statements which are open to criticism. To cite a few: "The cells themselves must be influenced ultimately by that mysterious force which we will call life, which ends with its extinction from the body as a whole and which is ultimately related to nerve action." The thyroid is said to be of great importance in governing the calcium metabolism. The same principles are said to hold good for the treatment of skin diseases and for cancer in general, because both concern aberrations in the behavior of epithelial cells; but internal organs like pancreas and liver, although they are of epithelial character, nevertheless do differ in their behavior from the skin. Postoperative recurrences of cancer are, according to the author, due to a transformation of formerly healthy cells into cancer cells as a result of faulty metabolism and not, as is almost generally assumed, to the incomplete removal of the original cancer.

LEO LOEB

The Cancer Problem. By William Seaman Bainbridge. The Macmillan Company, 1914.

Within the last decade several books have appeared dealing with the cancer problem; those of Carl Lewin, P. Menétrier, W. Roger Williams, W. H. Woglom, and the encyclopedic work of Jacob Wolff may be especially mentioned. Of those written in the English language, the book by Williams appeared seven years ago and Woglom's work treats mainly of experimental cancer research.

Dr. Bainbridge considers the cancer problem from many aspects; being a surgeon, however, the author devotes the greater part of his book to the clinical aspect of cancer (274 pages), while to the scientific side proper 142 pages are given. In the clinical part the author gives much first-hand experience, while in the scientific part he leans more or less on the judgment of others, especially on the writings of Bashford, and this part represents in part a summary of the reports of the English Cancer Research Fund. The book on the whole is well written and contains much interesting information. If in the following we mention a few of the errors which we find here and there, and take issue with some of the views expressed and with the author's treatment of certain aspects of scientific investigation, our purpose is not to detract from the value of the book as a whole.

In Section I. a survey of the various institutions and associations for the study of cancer is given. The American Association for Cancer Research did not come into existence in 1912 (p. 28), but was founded a number of years previously. On page 7 the "famous Althoff" who promised the aid of the government to the German Society for Cancer Research, is erroneously designated as "Kultus minister." The German society as such was not committed to the parasitic theory of the origin of cancer, for although some members supported this hypothesis, other important members, notably Orth and Von Hansemann, opposed it.

In Section II. we find a discussion of the botanical distribution of cancer. The analogy between crown gall and animal cancer is not accepted "since it presupposes the parasitic origin of cancer," and since "notably the presence of the parasites in Smith's secondary growths is in contradiction to the way in which secondary growths arise in man." In reality we can not be certain that even in man in certain tumors included among cancers, parasites are not within the tumor cells which give rise to the metastases. In the chapter on the zoological distribution, it is stated that the evidence is conclusive that benign as well as malignant tumors may occur in any multicellular organism. Whether typical cancer occurs at all in invertebrates is doubtful; certainly in the large majority of classes of invertebrates no cancer has been found. Carcinoma of the caruncula seems to be the most common site of cancer in cattle in various parts of America, not only in Wyoming, as might be inferred from the author's statement.

As to the ethnological distribution and cancer statistics the probabilities are very great indeed that the cancer rate among the African negro, the natives of Guinea and the American Indian is considerably lower than among the whites in Europe and America. The especially interesting data of Levin concerning cancer among the American Indian are not mentioned by the author. The value of possible objections to the conclusion that the cancer incidence is very different in different races seems to be overestimated. The author accepts as correct Murray's work on heredity of cancer in mice, which leads to the conclusion that heredity is responsible for a difference of only 10 to 15 per cent. in the cancer incidence in mice; in common with Bashford he attributes therefore only slight importance to the factor of heredity. As a matter of fact Murray's work is based on false premises and it proves neither the presence nor the absence of hereditary factors. Bainbridge makes no mention of more recent investigations carried on in Granby, Mass., and in Chicago, which indeed prove the great significance of heredity in cancer of mice, accounting for as great a

difference as 90 per cent. between some strains.

In Section IV. the various hypotheses concerning the origin of cancer and in a second chapter the predisposing causes are discussed. Ehrlich's "atreptic theory" ought to have been included in the first chapter; it is, as far as the etiology of cancer is concerned, a mere hypothesis and not one of the "predisposing causes." Long-continued action of Roentgen rays might almost be considered as "essential" and not merely a "predisposing" cause, if we bear in mind the great number of early Roentgen-ray operators who developed cancer of the exposed skin. The argumentation of C. P. White, apparently refuting as unthinkable a parasitic origin of cancer, is given in detail. Notwithstanding this argumentation, certain sarcomata of fowl which in their behavior seem to be distinguishable from human sarcomata, may perhaps be caused by microorganisms.

The section in histopathology contains a series of clear drawings. The description is of necessity brief. The purely local origin of cancer is emphasized. The origin of rodent ulcer is declared to be still uncertain, despite the fact that recent investigations have undoubtedly shown that in certain cases at least it originates in the epidermis.

Section VI. deals with "Cancer Research — a Résumé of the World's Work." The author has in view especially experimental research. Thirty-six pages are devoted to this chapter. Here we have to deal mainly with a résumé of the work of the English Cancer Research Fund. American work is to a great extent ignored. Not rarely when a fact established by an American author is mentioned, the author's name is not mentioned, so that a reader unfamiliar with the history of cancer research would be inclined to attribute the work to the English cancer research and to conclude that American research played a very subordinate part in this field. Such an assumption, however, would be incorrect, and it is to be deplored that much of the important work of Tyzzer, Gaylord, Flexner and Jobling, Weil, Levin, Sweet, Corson-White and Saxon, Fleisher and others is not mentioned. Peyton Rous's name is omitted in the brief reference to his work in this chapter. The early work on Chicago rat sarcoma is entirely omitted, although the survival of the tumor cells after transplantation had been demonstrated at an early period of this investigation.

It is not possible to go into a detailed criticism of some of the views expressed in this chapter; we may mention, however, a few statements with which issue might be taken. Bashford's and Murray's views as to the rhythm of tumor cells is accepted as proven; the work of other investigators (especially M. S. Fleisher) who arrived at different conclusions, is ignored. It is taken for granted that tumor cells differ from ordinary tissue cells in their potential power of unlimited growth, while on the contrary this characteristic is common to both kinds of cells and the difference consists essentially in the increase in cell multiplication in the case of tumor cells, as the reviewer pointed out many years ago. The fact that animals can, through immunization, be protected against successful inoculation with foreign, but not with their own tumors, is erroneously assumed to prove that no external element can be concerned in the origin of cancer, while this fact merely proves that an organism usually can be immunized much more readily against foreign cells than against its own, and also that in the first origin of tumors other factors are concerned than in the continued growth of established tumors. No conclusion can be drawn from this fact as to the presence or absence of parasites within the tumor cell. The work of Uhlenhuth which to a great extent disposes definitely of the hypothesis of athrepsia, is not mentioned.

In the second part, dealing with the clinical aspect of cancer, the clinical course of the disease, diagnosis, prophylaxis, treatment by surgical and non-surgical means, are discussed. Various quack treatments are also described. Especial attention is given to Handley's work dealing with the extension of mammary cancer, to the fulguration treatment and thermoradiotherapy of de Keating

Hart, to electro-coagulation and to the author's negative results with Beard's methods of treating cancer with injections of pancreatic ferments, as well as to the author's method of starvation ligature of blood vessels and lymphatic block in advanced cancer of pelvic organs. The wide experience of the author in this field, his insistence on applying the results of theoretical research in clinical surgery, give especial value to this, the larger part of the book. This work ought therefore to have a wide circulation especially among physicians. Here it can do much good. To the scientist who will keep in mind some of the limitations of this book, it will give a conception of the great variety of problems and methods in cancer research.

Leo Loeb
Washington University

The Age of the Ocala Limestone. By Charles Wythe Cooke. U. S. Geol. Surv., Prof. Paper 95–1, 1915. Pp. 107–117.

In the first half of the last century it was assumed by American geologists of the Atlantic seaboard that certain extensive calcareous formations in the Carolinas represented terranes intermediate between the Cretaceous and lowest Tertiaries of Europe, or, perhaps were "newest Cretaceous." This assumption seems to have been made on account of the prevalence of light-colored, calcareous matter, chalk, in the upper Cretaceous of the Old World; the lithological resemblance of certain Cretaceous beds in New Jersey to calcareous beds of the south; the supposed identity of certain molluscan species from both areas; and the admixture of fossils from different horizons (really brought about mechanically, or from careless collecting). Lyell took a keen interest in this strange formation in America, and with his skill in observation "on the spot," was able to place these "white limestones" in the Eocene, to the satisfaction of all.

Again in our Eocene stratigraphy we see how a few accurate observations in the field have upset our notions regarding sequence of formations; this time, however, it is the "Ocala limestone" so-called (yet strangely enough largely equal to Lyell's "white limestone"), that has been the misplaced member. Here, too lithological resemblance, preconceived notions in faunal resemblances and unhappy identifications have been at the base of the trouble. Mr. Cooke's observations on the fauna of the beds beneath the St. Stephen's limestone in Alabama, has led to the identification of the same with the Ocala beds of Florida. The preliminary paleontological proof he brings to bear in favor of his contention seems very satisfactory. The Ocala limestone, therefore, is upper Eocene (Jacksonian) and below the Marianna limestone, and not upper Oligocene and above the Marianna as heretofore held. The importance of this revelation on the geological mapping of Florida is patent to all. We take great pleasure in seeing the distinctness of *Pecten poulsoni* and *P. perplanus* biologically and stratigraphically emphasized. The "Ocala limestone fauna" as modified by Cooke (p. 111) has a most decidedly Jacksonian aspect. The "*Mitra* like *millingtoni*" is quite probably that species for I have found it above the Claiborne "sand" at Claiborne, Alabama, thus well on towards Florida from Jackson, Miss. *Scaphander grandis* is a most remarkably characteristic Jacksonian form. Judging by trans-Mississippian faunas, we should expect soon to find in the Ocala such dominant forms as the Fulguroid *Levifusus branneri,* varieties of *Mazzalina inaurata;* and we already have traces of the high-spired "*Amauropsis*" in Dall's *A. ocalana.* Incidentally, with the Jackson age of the Wilmington beds established, it will be interesting to watch the final disposition of the following references:

Paludina (cast), Wilmington, Jr. Geol. Soc. Lond., Vol. 1, 1845, p. 431, text fig. *c.*

Viviparia lyelli Con., Am. Jr. Conch., Vol. 1, 1865, p. 32.

Polynices (*Amauropsis*) *ocalana,* Dall, Tr. Wagner, Ins. Sci., Vol. III., 1892, p. 377.

Amauropsis Jacksonensis Harris, Proc. Phila. Acad. Nat. Sci., 1896, p. 474, pl. XIX., fig. 3.

G. D. Harris
Paleontological Laboratory,
Cornell University

SPECIAL ARTICLES

PERIDERMIUM HARKNESSII AND CRONARTIUM QUERCUUM

INOCULATIONS of *Pinus radiata* with æciospores of *Peridermium harknessii* on *Pinus radiata* made in the spring of 1913 resulted in typical galls during the same year. In the spring of 1915 some of these galls bore æcia of *Peridermium harknessii*. The check plants remained sound.

The mycelium of *Cronartium quercuum* on the evergreen *Quercus agrifolia* overwinters in the old green leaves and in early spring produces sori of uredospores in a circle around the old *Cronartium* spots; the uredinial sori on the young leaves are the results of infection from the sori on the old leaves. If *Peridermium harknessii* connects with *Cronartium quercuum*, we have here a case of facultative heteroecism in both generations.

E. P. MEINECKE

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SAN FRANCISCO, CALIF.

A SIMPLE DEMONSTRATION OF THE REDUCED VAPOR PRESSURE OVER A SOLUTION

W AND *S* are two small glass crystallizing dishes. *W* is half filled with water and *S* with a strong solution of some salt. *P* is a piece of

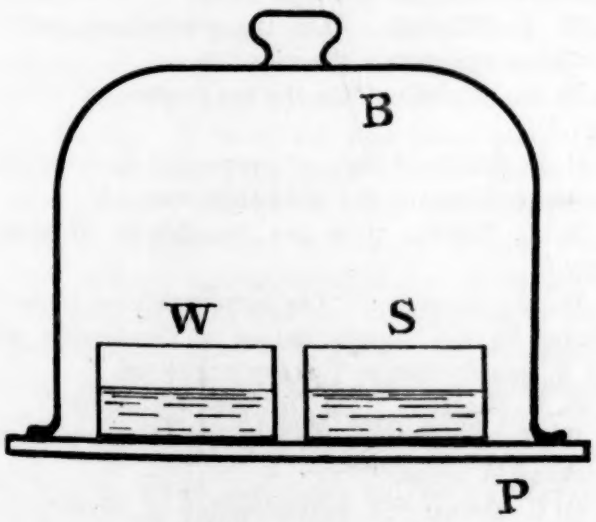

plate glass and *B* is a bell jar. For equilibrium the pressure of the vapor above *S* would have to be less than that above *W*. For this reason the water gradually distills from *W* into *S*.

This result is so obvious that the experiment has no doubt been carried out before. However in a recent brief examination of the literature of the reduction of vapor pressure by solution I have found no reference to it, although Moser[1] clearly indicates the possibility of such an experiment. In his work he used two U tubes, one for the water and one for the solution. One end of each tube was closed, and the open ends were joined—so that with a connection to an air pump these open ends formed a fork. Moser says:

> Das Lumen dieses Gabelrohrs ist eng, ein bis zwei Millimeter, um eine Ueberdestilliren des Dampfes vom Wasser zur Lösung zu erschweren.

In my experiment, which I carried out three years ago, the dishes *W* and *S* were about 5 cm. in diameter and *S* contained a solution of about 1 g. of sodium chloride to each 5 g. of water. Vacuum wax was run around *B* where it rested on *P*, but no attempt was made to reduce the air pressure in *B*. The apparatus stood in a room at ordinary laboratory temperature from January 26 to March 21. At first I set out to examine the rate at which the liquid surfaces changed their levels, but the sides of *B* were not smooth enough to admit of making through them any readings that were worth while. At the start the levels were about the same, and after somewhat less than two months the surface of the solution was 9.0 mm. higher than that of the water.

ARTHUR TABER JONES

SMITH COLLEGE,
January 23, 1915

THE AMERICAN MATHEMATICAL SOCIETY

THE twenty-second annual meeting of the society was held at Columbia University on Monday and Tuesday, December 27–28, 1915. Seventy-two members attended the four sessions. President E. W. Brown occupied the chair, being relieved by Professor Edward Kasner. The following new members were elected: Professor W. E. Edington, University of New Mexico; Professor J. L. Gibson, University of Utah; Dr. W. E. Milne, Bowdoin College; Professor L. J. Reed, University of Maine. Nine ap-

[1] *Wied. An.*, 14, p. 73, 1881.

plications for membership were received for action at the next meeting.

The total membership of the society is now 736, including 72 life members. The total attendance of members at all meetings during the past year was 418; the number of papers read was 197. The number of members attending at least one meeting during the year was 253. At the annual election 204 votes were cast. The treasurer's report shows a balance of $10,470.58, including the life membership fund of $5,560.30. Sales of the Society's publications during the year amounted to $1,832.93. The library now contains about 5,250 volumes.

Sixty members and friends attended the annual dinner of the society on Monday evening.

At the annual election on Tuesday morning the following officers and members of the council were chosen:

Vice-Presidents: E. R. Hedrick and Virgil Snyder.

Secretary: F. N. Cole.

Treasurer: J. H. Tanner.

Librarian: David Eugene Smith.

Committee of Publication: F. N. Cole, Virgil Snyder, and J. W. Young.

Members of the Council to serve until December, 1918: G. A. Bliss, R. D. Carmichael, W. B. Fite, and F. S. Woods.

The following papers were read at this meeting:

J. F. Ritt: "On the derivatives of a function at a point."

J. F. Ritt: "The finite groups of a class of functions of a real variable."

J. E. Rowe: "A new method of deriving the equation of a rational plane curve from its parametric equations."

H. B. Phillips: "Elastic nets."

Arthur Ranum: "The singular points of analytic space curves."

H. M. Sheffer: "The reduction of non-monadic relations to monadic."

H. M. Sheffer: "The elimination of modular existence postulates."

Bessie I. Miller: "A new canonical form of the elliptic integral."

A. R. Schweitzer: "On the use of supernumerary indefinables in the construction of axioms."

Dunham Jackson: "Algebraic properties of self-adjoint systems."

G. D. Birkhoff: "On dynamical systems with two degrees of freedom."

G. D. Birkhoff: "Infinite products of analytic matrices."

Tomlinson Fort: "Linear difference and differential equations."

E. B. Wilson: "Ricci's absolute calculus and its application to the theory of surfaces."

C. L. E. Moore: "Some theorems regarding two-dimensional surfaces in euclidean n-space."

Olive C. Hazlett: "On the fundamental invariants of nilpotent algebras in a small number of units."

Edward Kircher: "Some properties of finite algebras."

M. Fréchet: "On Pierpont's definition of integrals."

Edward Kasner: "Infinite groups of conformal representations."

Joseph Lipka: "Isogonal, natural, and isothermal families of curves on a surface."

L. L. Silverman: "On the consistency and equivalence of certain generalized definitions of a limit of a function of a continuous variable."

L. P. Eisenhart: "Ruled surfaces generated by the motion of an invariable curve."

L. P. Eisenhart: "Transformations of surfaces Ω (second paper)."

G. M. Green: "On rectilinear congruences and nets of curves on a surface."

W. F. Osgood: "The infinite region."

John Eiesland: "On sphere-flat geometry."

J. L. Coolidge: "The meaning of Plücker's numbers for a real curve."

W. M. Smith: "Characterization of the trajectories described by a particle moving under central force varying inversely as the nth power of its distance from the center of force."

H. H. Mitchell: "On the generalized Jacobi-Kummer cyclotomic function."

H. H. Mitchell: "On the congruence $cx^{\lambda} + 1 = dy^{\lambda}$."

R. D. Beetle: "Sets of properties characteristic of the arithmetic and geometric means."

R. L. Moore: "On the foundations of geometry."

W. C. Graustein: "The correspondence of space curves by the transformation of Combescure and by a transformation thereby suggested."

R. E. Gleason: "On Dirichlet's principle."

W. E. Milne: "On the degree of convergence of Birkhoff's series."

G. C. Evans: "A generalization of Böcher's analysis of harmonic functions."

J. W. Alexander, II.: "On the factoring of plane Cremona transformations."

L. B. Robinson: "On elimination between several polynomials in several variables."

The Chicago Section of the society held its winter meeting at Columbus, Ohio, in affiliation with the American Association for the Advancement of Science. The next meeting of the society will be held at Columbia University on February 26.

F. N. COLE,
Secretary

SOCIETIES AND ACADEMIES

THE BIOLOGICAL SOCIETY OF WASHINGTON

THE 545th meeting of the society was held in the Assembly Hall of the Cosmos Club, Saturday, November 20, 1915, called to order by President Bartsch, with 50 persons present.

On recommendation of the council Leo D. Miner, E. O. Wooten, A. M. Groves, all of Washington, D. C., were elected to active membership.

Under the heading Brief Notes, Mr. Radcliffe called attention to recent efforts of the Bureau of Fisheries in rearing shad in ponds. Young fish thus raised attained twice the size of those of the same age in their natural environment. Specimens of both kinds were exhibited.

The first paper of the regular program was by Frederick Knab, "The Dispersal of Some Species of Flies." Mr. Knab said: "The species of Diptera that have been spread beyond their natural habitats through the agency of man are for the most part such as thrive under conditions created by man, many of them having even become his inseparable associates. They are mostly scavengers whose larvæ thrive in spoiled foodstuffs, sewage and excrement of man or domestic animals. The majority of the flies of such habits occurring in North America are unintentional introductions from Europe. It is certain that many other species of flies must have been carried across the ocean repeatedly and yet failed to establish themselves. It is only those species which upon their arrival find conditions suitable for propagation immediately at hand that can be expected to gain a foothold, and most of these will be scavengers. A few striking examples of the wide dissemination of such species by man were given.

"A notable case is the very wide distribution of *Eristalis tenax*, the drone fly, within very recent times. Its natural habitat was Europe, northern Africa and the temperate portions of Asia. It appears to have been first noted in the United States about 1870 and in the course of a decade had spread over the whole country and become abundant everywhere. Osten Sacken already pointed out that its sudden spread was only possible 'when the necessary conditions for its existence (drains, cesspools, sewers, etc.) had been gradually introduced by civilization across the immense plains which separate the Pacific from the Atlantic Ocean.' Most remarkable is that this fly made its appearance in New Zealand in 1888, where the following year it was abundant in both islands. In America and elsewhere *Eristalis tenax* has not invaded the tropics. In North America it ranges southward on the Mexican tableland to Mexico City and even to Orizaba at the edge of the tropical belt. But in the temperate southern portion of South America it has become established with the recent more general settling up of that region. It was first noted at Buenos Aires about 1895 and is now abundant and generally distributed to the Chilean coast. It has become introduced in Cape Colony and the Hawaiian Islands, the records for the latter going back to 1892. It is also established in southern Australia and appears to have been common about Sydney as early as 1892.

"A second species, *Eristalis arbustorum*, has recently become introduced into the United States from Europe. Like the other, it is a sewage breeder. It was first noticed about New York City in 1906 and has already spread westward through Ohio.

"Another recent importation from Europe is the ortalid fly, *Chrysomyza demandata*. This species breeds particularly in horse manure. It was first found in Philadelphia in 1897 and is now distributed over the whole United States.

"Less known are the species which have become cosmopolitan within the tropics, but do not invade the colder portions of the temperate zone. *Volucella obesa* is a large green syrphid fly of scavenger habits. Its original habitat was tropical America, but now it is generally distributed through the tropics of the Eastern Hemisphere, occurring even on remote islands, like Hawaii and Guam.

"A minute fly of the family Borboridæ, *Leptocera punctipennis* Wied. (*Borborus venalicius* O. S.) is similarly distributed. Osten Sacken, who knew of its occurrence in Africa and Cuba, suggested that it may have been brought to America by slave ships. This theory appears plausible, as it has since been determined that this fly breeds particularly in human feces deposited in the open. During the Spanish-American war it appeared in numbers at Miami, Florida, about the military camp, and where, no doubt, the conditions just indicated

existed. It has not been reported from there since, although the locality is often visited by entomologists.

"*Chrysomyza ænea*, a fly common in the Orient and breeding especially in manure, is of particular interest on account of its very recent appearance within the United States. It was first found in August of this year and so far only in one locality in Louisiana. It appears to have been established in Brazil for some time and very likely occurs in intervening territory, although we have no information on this latter point.

"Another cosmopolite of tropical and semi-tropical distribution is *Milichiella lacteipennis*, a minute fly of the agromyzid series. This also, there is good reason to believe, is a manure breeder.

"A limited number of species are disseminated through both temperate and tropical regions. The house fly, stable fly and certain species of *Drosophila* will at once come to mind as faithful companions of man everywhere. Most remarkable, there is in this category a minute and very frail fly of the family Psychodidæ, *Psychoda alternata*. The flight of this mere mote is exceedingly weak and it clings to sheltered situations. It breeds particularly in sewage and often occurs in sewers in countless numbers. This fly has been received or reported from Europe, North Africa, the United States, Mexico, Guiana, Chile, Hawaii, India and Australia, and no doubt it occurs whenever a sufficiently dense population supplies the requisite conditions."

The second paper was by Alex. Wetmore, "Notes on the Habits of the Duck Hawk." Mr. Wetmore said: "In observations made on the Bear River marshes, Great Salt Lake, Utah, it was found that duck hawks do much of their hunting for food in early morning. Later in the day they pursue any flying bird merely for the pleasure of the chase, seldom killing." Several incidents illustrating this were related.

The last paper of the evening was by Elmer D. Merrill, "Geographic Relationships of the Philippine Flora." Mr. Merrill based his conclusions after the examination of large numbers of living and herbarium specimens from the Philippine Islands, the Malayan Archipelago, the Asiatic mainland, Celebes, New Guinea, Australia, etc. The speaker discussed, in a general way, the geographic position of the Philippine Archipelago with reference to surrounding land areas and the general character of the flora, calling attention to the fact that the vegetation is dominantly Malayan. The probable condition of the vegetation before the advent of man in the Archipelago was a continuous primeval forest. Hence in discussing geographic relationships of the flora, the vegetation of the settled areas and open country generally must be excluded from consideration as presenting special alliances. Likewise the coastal vegetation must be ignored, the species being practically all disseminated by ocean currents. Serially the speaker discussed the striking Asiatic elements in the flora of north central Luzon, largely continental and especially Himalayan foothill types; the weak special alliances of the Sunda group of islands, especially Borneo; the remarkably strong evidences of relationship with the Molucca Islands, especially Celebes, to the south; New Guinea; the numerous Australian (Queensland) types; New Zealand, and Polynesia. The botanical evidence points to weak connections in past ages with Borneo and the Sunda Islands, but to strong or longer continued connections with the islands to the south and southeast. Without such conections to the south and southeast it is practically impossible to explain the strong special alliances of the flora to that of the above regions. That the Philippines and the islands to the south and southeast may have at one time formed the eastern boundary of an ancient continent seems to be probable from the present floristic elements found in the archipelago. It is clear, however, from the remarkably high percentage of endemism as to species (over 50 per cent.) that the islands have been separated long enough to allow for the development of a characteristic flora as to species, but not long enough to develop many distinct genera, the percentage of endemism as to genera being but a fraction of one per cent.

The speaker called attention to the fact that conclusions regarding special alliances of the Philippine flora may be invalidated as exploration progresses, as the floras of Sumatra, Borneo, the Moluccas, and New Guinea, are, comparatively speaking, very imperfectly known, in the case of each probably not more than one third of the species being known, and in some cases even less.

In the discussion which followed Mr. Wm. Palmer, Dr. Stejneger, Dr. Lyon, and Dr. Bartsch discussed the geographic distribution of the Philippine birds, reptiles, mammals and mollusks, which in many respects showed a lack of correlation with the flora, though agreeing in many essentials.

The society adjourned at 10:30 P.M.

M. W. Lyon, Jr.,
Recording Secretary